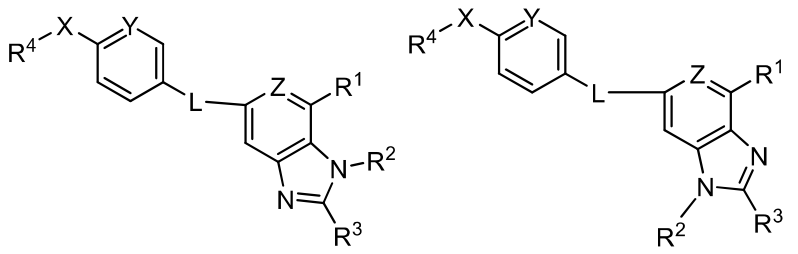
SUMMARY

[0004] In one aspect, the present disclosure provides a compound of formula (I) or formula (Ia):



(I) or (Ia),

or a pharmaceutically acceptable salt or tautomer thereof,

wherein:

Lis -C(O)NH-, -NHC(O)-, -NHS(O)$_2$-, or -S(O)$_2$NH-;

X is -O- or -S-;

Y is CH, C(halo), C(C_1-C_2 alkyl), or N;

Z is CR^5 or N;

R^1 is $C(O)NR^6R^7$, $C(O)OR^6$, $NR^6C(O)R^7$, $NR^6S(O)_2R^7$, $S(O)_2NR^6R^7$, 4-10 membered heterocyclyl, C_6-C_{10} aryl, or 5-10 membered heteroaryl, wherein the 4-10 membered heterocyclyl, C_6-C_{10} aryl, and 5-10 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, CN, C_1-C_6 alkyl, OH, OC_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

R^2 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, or 5-10 membered heteroaryl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, and 5-10 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of oxo, halo, CN, C_1-C_6 alkyl, C(O)NHC_1-C_6 alkyl, (O)NHC_3-C_6 cycloalkyl, OH, OC_1-C_6 alkyl, C_3-C_6 cycloalkyl, and 4- to 6-membered heterocyclyl;

R^3 is:

(i) H, NR^6R^7, or OR^6;

(ii) C_1-C_6 alkyl optionally substituted with 1-3 substituents selected from the group consisting of halogen, hydroxyl, and –O(C_1-C_6 alkyl); or

(iii) C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 4- to 6-membered heterocycloalkyl, C_6-C_{10} aryl, or 5- to 10-membered heteroaryl, wherein the C_2-C_6 alkenyl, C_2-C_6 alkynyl,

C_3-C_6 cycloalkyl, 4- to 6-membered heterocycloalkyl, C_6-C_{10} aryl, and 5- to 10-membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1-C_6 alkyl and OH; or

R^2 and R^3, together with the intervening atoms to which they are attached, form a 4-10 membered heterocycloalkyl, wherein the 4-10 membered heterocycloalkyl is optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-OH, C(O)C_1-C_6 alkyl, and OH;

R^4 is C_1-C_6 alkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, and C_2-C_6 alkynyl are each optionally substituted with 1, 2, or 3 independently selected halo substituents;

R^5 is H or halo;

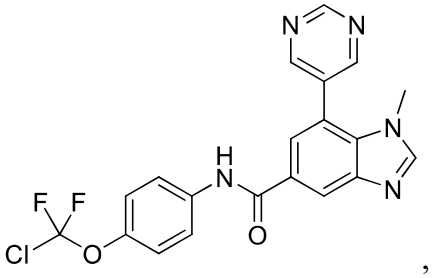
R^6 is H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, or 5-10 membered heteroaryl, wherein the C_1-C_6 alkyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, and 5-10 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1 -C_6 alkyl, and OH; and

R^7 is H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C6-C_{10} aryl, or 5-10 membered heteroaryl, wherein the C_1-C_6 alkyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, and 5-10 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1-C_6 alkyl, and OH; or

R^6 and R^7, together with the nitrogen atom to which they are attached, form a 4-7 membered heterocyclyl, wherein the 4-7 membered heterocyclyl is optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1-C_6 alkyl, and OH;

with the proviso that the compound is not:

[0004g] In another aspect, the present disclosure provides a compound selected from the group consisting of: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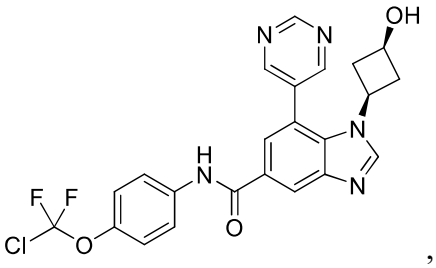
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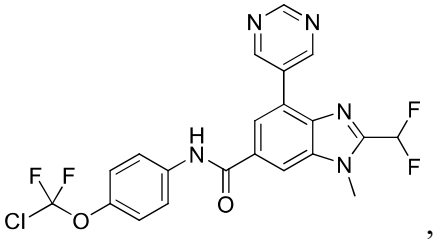
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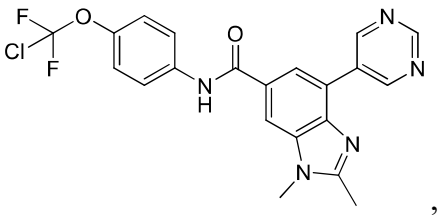
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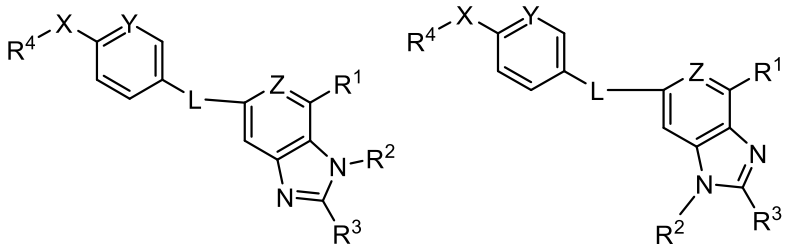
WHAT IS CLAIMED IS:

1. A compound of formula (I) or formula (Ia):



(I) or (Ia),

or a pharmaceutically acceptable salt or tautomer thereof,

wherein:

Lis -C(O)NH-, -NHC(O)-, -NHS$(O)_2$-, or -S$(O)_2$NH-;

X is -O- or -S-;

Y is CH, C(halo), C(C_1-C_2 alkyl), or N;

Z is CR^5 or N;

R^1 is C(O)NR^6R^7, C(O)OR^6, NR^6C(O)R^7, NR^6S$(O)_2R^7$, S$(O)_2NR^6R^7$, 4-10 membered heterocyclyl, C_6-C_{10} aryl, or 5-10 membered heteroaryl, wherein the 4-10 membered heterocyclyl, C_6-C_{10} aryl, and 5-10 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, CN, C_1-C_6 alkyl, OH, OC_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

R^2 is H, C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, or 5-10 membered heteroaryl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, and 5-10 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of oxo, halo, CN, C_1-C_6 alkyl, C(O)NHC_1-C_6 alkyl, (O)NHC_3-C_6 cycloalkyl, OH, OC_1-C_6 alkyl, C_3-C_6 cycloalkyl, and 4- to 6-membered heterocyclyl;

R^3 is:

(i) H, NR^6R^7, or OR^6;

(ii) C_1-C_6 alkyl optionally substituted with 1-3 substituents selected from the group consisting of halogen, hydroxyl, and –O(C_1-C_6 alkyl); or

(iii) C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 4- to 6-membered heterocycloalkyl, C_6-C_{10} aryl, or 5- to 10-membered heteroaryl, wherein the C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 4- to 6-membered heterocycloalkyl, C_6-C_{10} aryl, and 5- to 10-membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1-C_6 alkyl, and OH; or

R^2 and R^3, together with the intervening atoms to which they are attached, form a 4-10 membered heterocycloalkyl, wherein the 4-10 membered heterocycloalkyl is optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-OH, C(O)C_1-C_6 alkyl, and OH;

R^4 is C_1-C_6 alkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, and C_2-C_6 alkynyl are each optionally substituted with 1, 2, or 3 independently selected halo substituents;

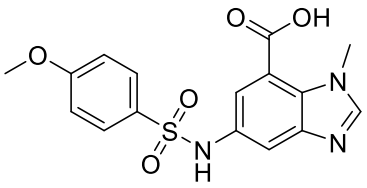
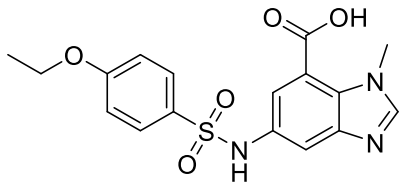
R^5 is H or halo;

R^6 is H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, or 5-10 membered heteroaryl, wherein the C_1-C_6 alkyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, and 5-10 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1 -C_6 alkyl, and OH; and

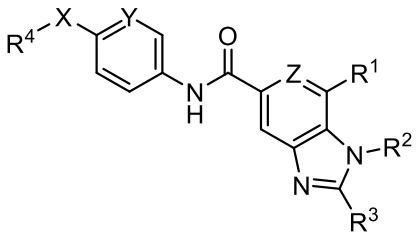
R^7 is H, C_1-C_6 alkyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C6-C_{10} aryl, or 5-10 membered heteroaryl, wherein the C_1-C_6 alkyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, and 5-10 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1-C_6 alkyl, and OH; or

R^6 and R^7, together with the nitrogen atom to which they are attached, form a 4-7 membered heterocyclyl, wherein the 4-7 membered heterocyclyl is optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1-C_6 alkyl, and OH;

with the proviso that the compound is not:

(i)  or (ii)  .

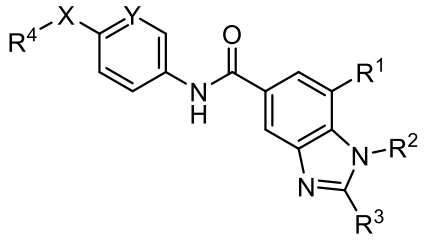
2. The compound of claim 1, wherein the compound is of formula (IA-1):

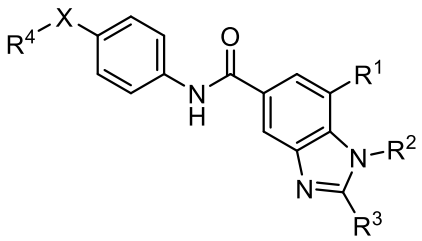


(IA-1) ,

or a pharmaceutically acceptable salt or tautomer thereof.

3. The compound of claim 2, wherein the compound is of formula (IIA), formula (IIB), formula (IIC), formula (IID), formula (IIE), formula (IIF), formula (IIG), or formula (IIH):



(IIA) , 

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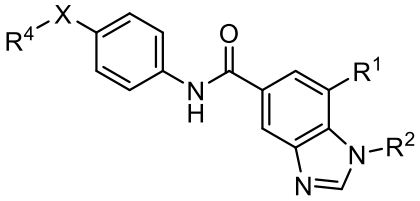
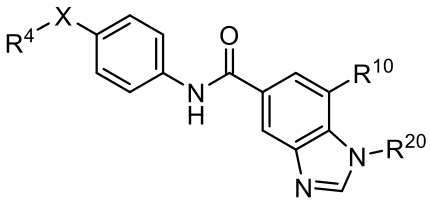
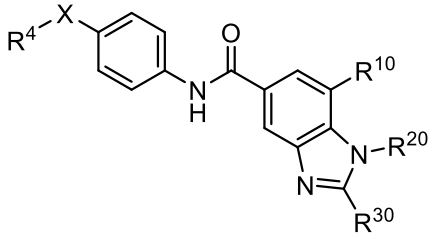
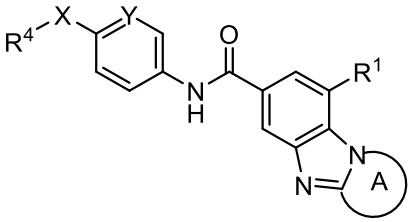


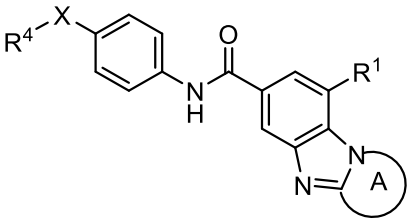
(IIC) , 

(IID) ,

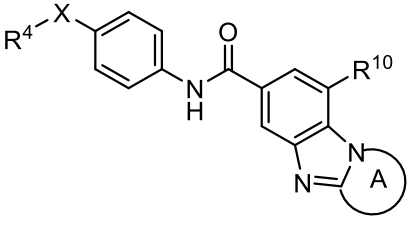


(IIE) ,



(IIF) , 

(IIG) ,



(IIH)

or ;

or a pharmaceutically acceptable salt or tautomer thereof,

wherein:

R^{10} is 5-6 membered heteroaryl, optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, CN, C_1-C_6 alkyl, OH, OC_1-C_6 alkyl, and C_3-C_6 cycloalkyl;

R^{20} is C_1-C_3 alkyl, C_3-C_4 cycloalkyl, or 4-6 membered heterocycloalkyl, wherein the C_1-C_3 alkyl, C_3-C_4 cycloalkyl, and 4-6 membered heterocycloalkyl are each optionally substituted substituted with 1, 2, or 3 substituents independently selected from the group consisting of oxo, halo, CN, C_1-C_6 alkyl, $C(O)NHC_1$-C_6 alkyl, $C(O)NHC_3$-C_6 cycloalkyl, OH, OC_1-C_6 alkyl, C_3-C_6 cycloalkyl, and 4- to 6-membered heterocyclyl;

R^{30} is H, C_1-C_3 alkyl, C_3-C_4 cycloalkyl, or 5-6 membered heterocycloalkyl, wherein the C_1-C_3 alkyl, C_3-C_4 cycloalkyl, or 5-6 membered heterocycloalkyl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1-C_6 alkyl, and OH; and

Ring A is 5-6 membered heterocycloalkyl, optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of oxo, C_1-C_6 alkyl, C_1-C_6 haloalkyl, C_1-C_6 alkyl-OH, $C(O)C_1$-C_6 alkyl, and OH.

4. The compound of claim 3, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^{30} is C_1-C_3 alkyl, C_3-C_4 cycloalkyl, or 5-6 membered heterocycloalkyl, wherein the C_1-C_3 alkyl, C_3-C_4 cycloalkyl, or 5-6 membered heterocycloalkyl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1-C_6 alkyl, and OH.

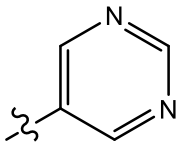
5. The compound of claim 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein X is -O-.

6. The compound of claim 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein Y is CH.

7. The compound of claim 3, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^1 is 4-10 membered heterocyclyl or 5-10 membered heteroaryl, wherein the 4-10

membered heterocyclyl and 5-10 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, CN, C_1-C_6 alkyl, OH, OC_1-C_6 alkyl, and C_3-C_6 cycloalkyl.

8. The compound of claim 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^1 is -$C(O)NH_2$, $C(O)NHCH_3$, C(O)NH(cyclopropyl),



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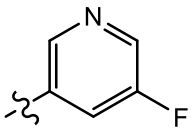

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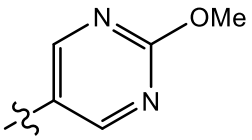

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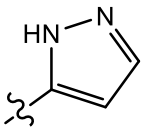

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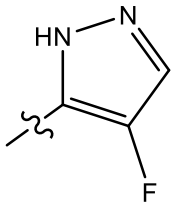

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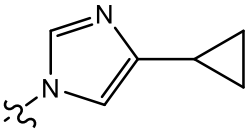

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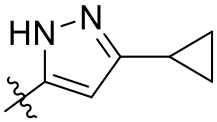

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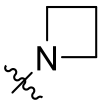

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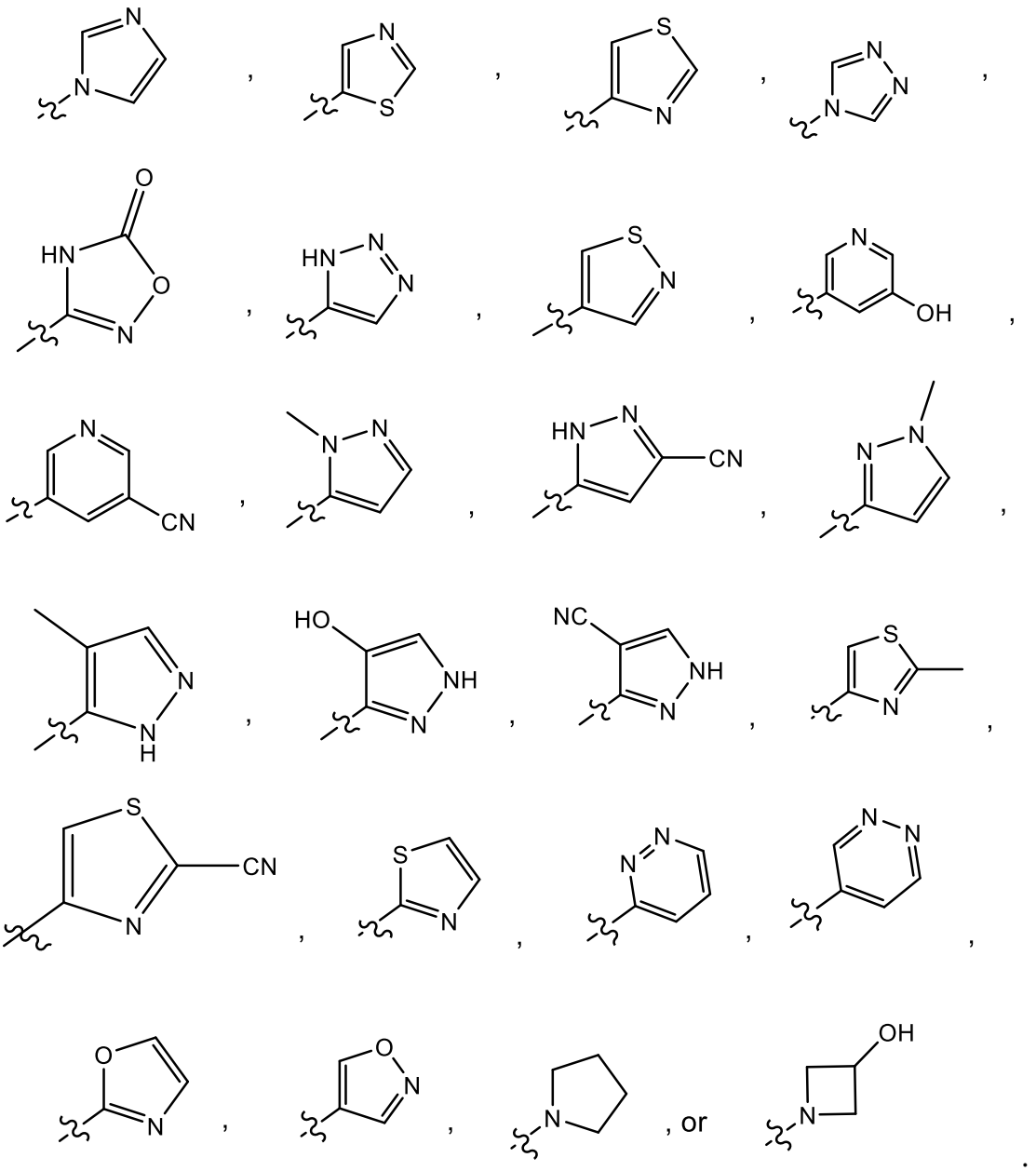
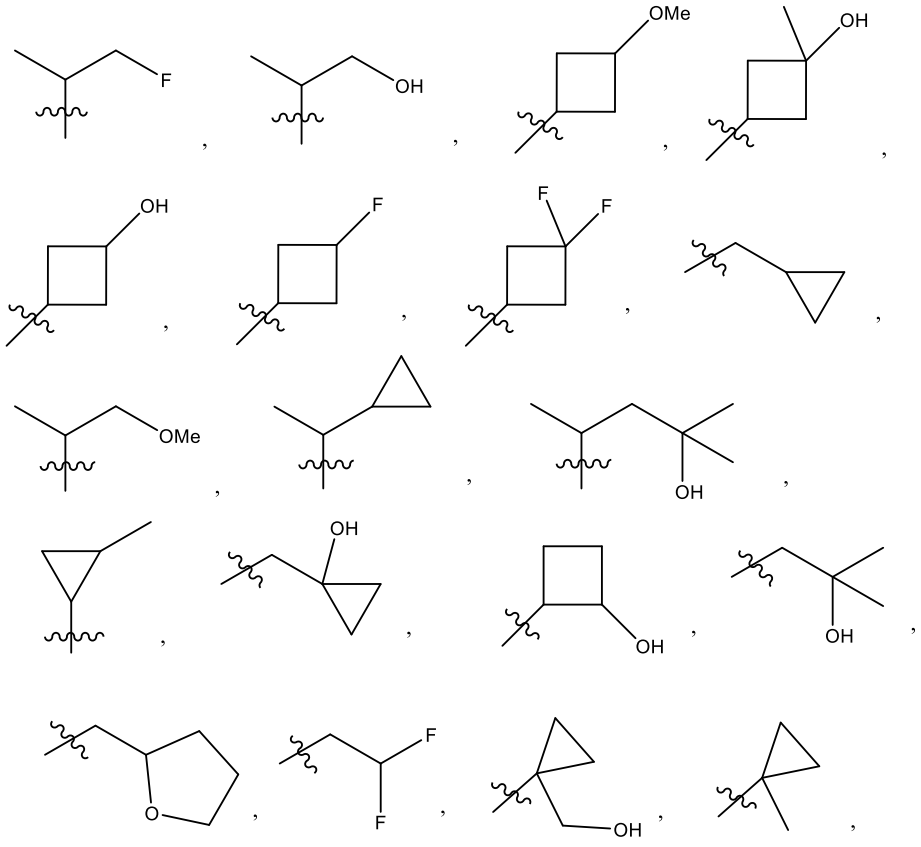


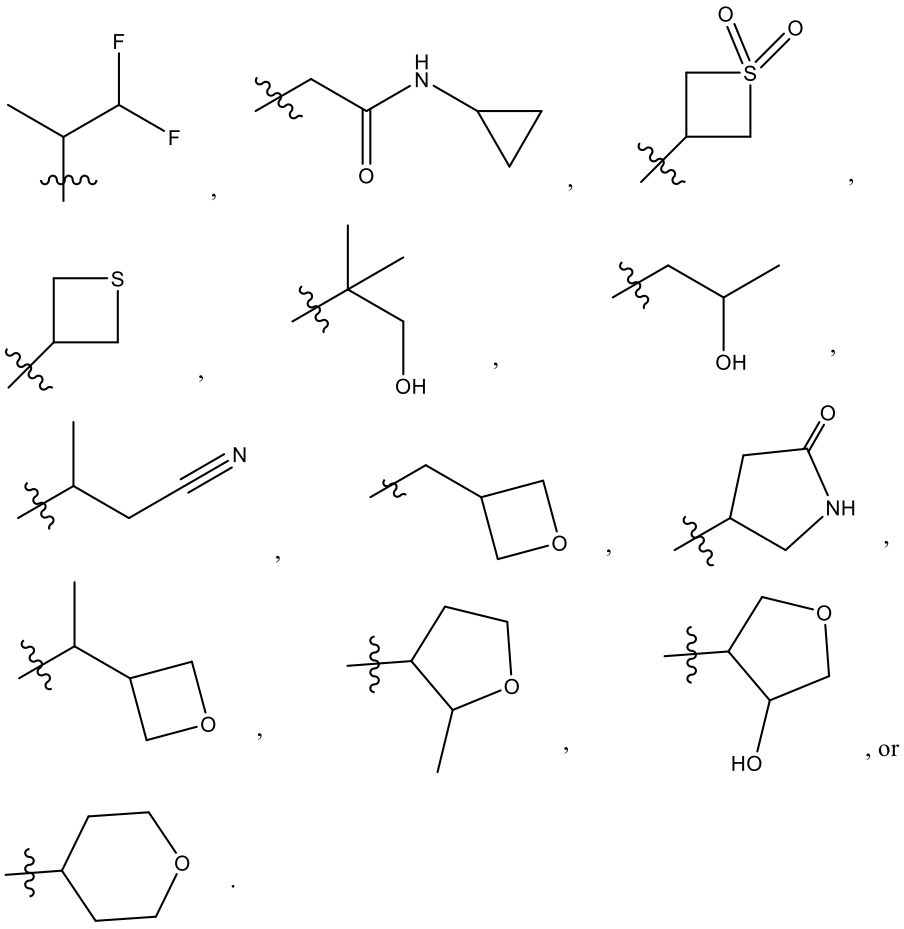
9. The compound of claim 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^1 is pyrazolyl or pyrimidinyl, wherein the pyrazolyl and pyrimidinyl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, CN, C_1-C_6 alkyl, OH, OC_1-C_6 alkyl, and C_3-C_6 cycloalkyl.

10. The compound of claim 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^2 is C_1-C_3 alkyl or C_3-C_4 cycloalkyl, wherein the C_1-C_3 alkyl and C_3-C_4 cycloalkyl are each optionally substituted with 1, 2, or 3 substituents independently selected from the

group consisting of oxo, halo, CN, C_1-C_6 alkyl, C(O)NHC_1-C_6 alkyl, C(O)NHC_3-C_6 cycloalkyl, OH, OC_1-C_6 alkyl, C_3-C_6 cycloalkyl, and 4- to 6-membered heterocycly 1.

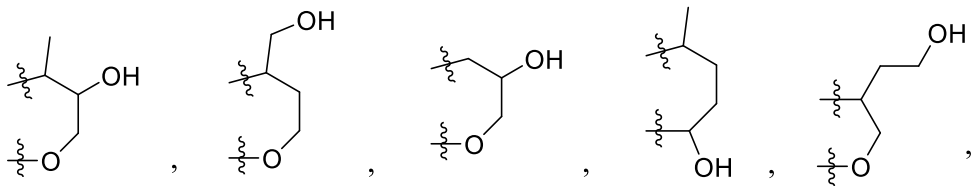
11. The compound of claim 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^2 is CH_3, CH_2CH_3, $CH(CH_3)_2$, $C(CH_3)_3$, cyclopropyl, cyclobutyl, cyclopentyl, tetrahydrofuranyl, tetrahydropyranyl,

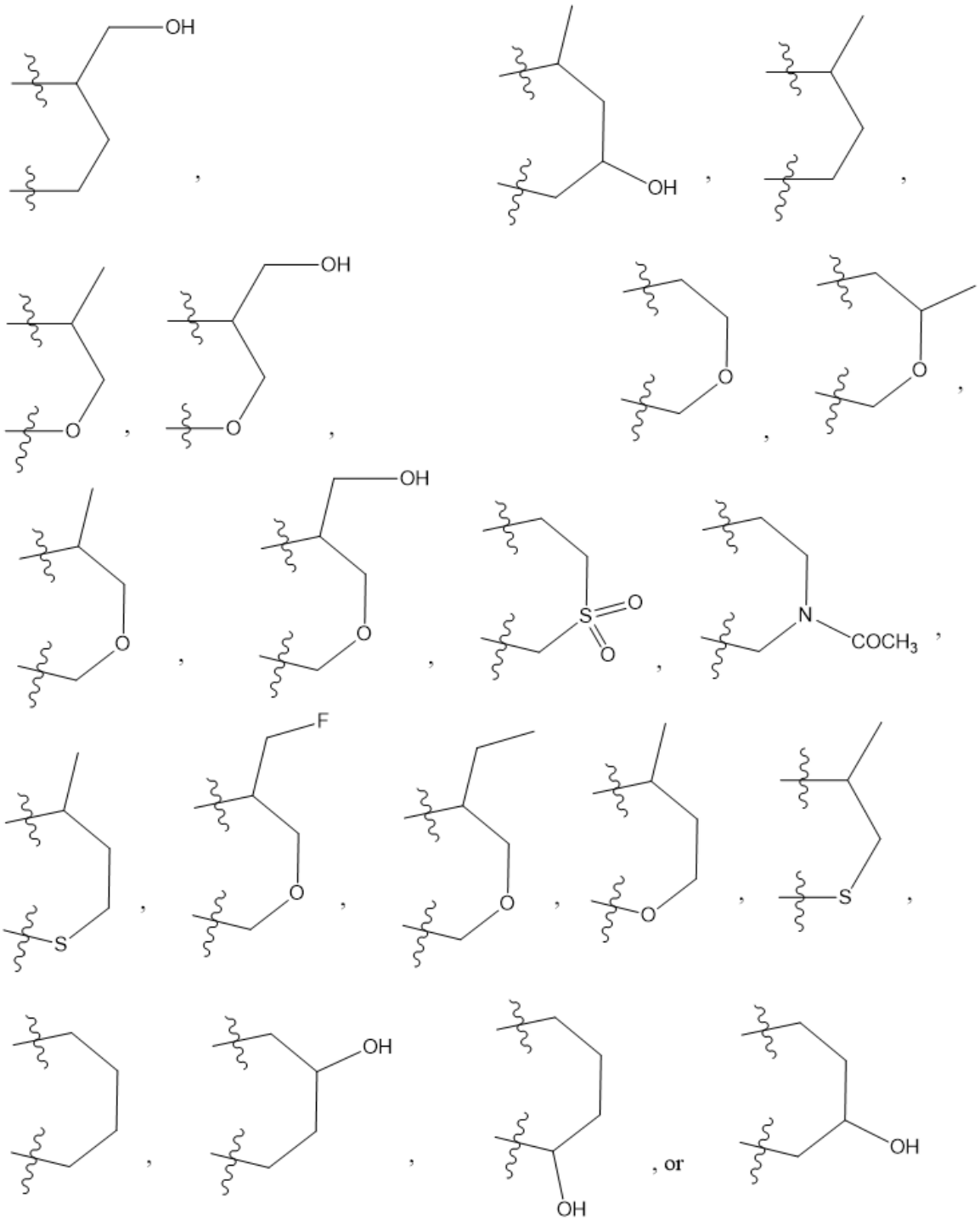




12. The compound of claim 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^3 is H, CH_3, CHF_2, CH_2OH, CH_2OCH_3, CH_2CH_2OH, $CH(CH_3)QH$, $CH(CH_3)_2$, $C(CH_3)_2OH$, OCH_3, OCH_2CH_3, cyclopropyl, cyclobutyl, or tetrahydropyranyl.

13. The compound of claim 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^2 and R^3 together form:



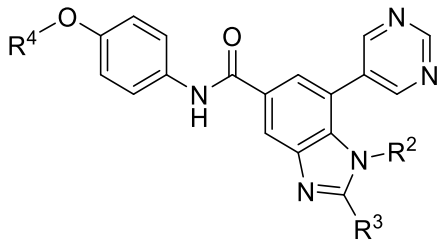


14. The compound of claim 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^4 is C_1-C_3 alkyl, optionally substituted with 1, 2, or 3 independently selected halo substituents.

15. The compound of claim 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^4 is CF_3 or CF_2Cl.

16. The compound of claim 2, or a pharmaceutically acceptable salt or tautomer thereof, wherein R^5 is H.

17. The compound of claim 2, wherein the compound is of formula (Id) or formula (Ie):



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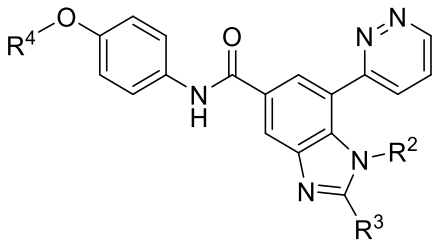


(Id) (Ie)

or a pharmaceutically acceptable salt or tautomer thereof.

18. The compound of claim 1, or a pharmaceutically acceptable salt or tautomer thereof, wherein:

R^1 is 4-10 membered heterocyclyl, C_6-C_{10} aryl, or 5-10 membered heteroaryl, each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, CN, C_1-C_6 alkyl, OH, OC1-C6 alkyl, and C_3-C_6 cycloalkyl;

R^2 is C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, or 5-10 membered heteroaryl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, and 5-10 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of oxo, halo, CN, C_1-C_6 alkyl, C(O)NHC_1-C_6 alkyl, C(O)NHC_3-C_6 cycloalkyl, OH, OC_1-C_6 alkyl, C_3-C_6 cycloalkyl, and 4- to 6-membered heterocyclyl;

R^3 is C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 4- to 6-membered heterocycloalkyl, C_6-C_{10} aryl, or 5- to 10-membered heteroaryl, wherein the C_2-C_6 alkenyl, C_2-C_6 alkynyl, C_3-C_6 cycloalkyl, 4- to 6-membered heterocycloalkyl, C_6-C_{10} aryl, and 5- to

10-membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1-C_6 alkyl, and OH; or

R^2 and R^3, together with the intervening atoms to which they are attached, form a 4-10 membered heterocycloalkyl, wherein the 4-10 membered heterocycloalkyl is optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of oxo, C_1-C_6 alkyl, C_1-C_6 alkyl-OH, C(O)C_1-C_6 alkyl, and OH;

R^4 is C_1-C_6 alkyl, C_2-C_6 alkenyl, or C_2-C_6 alkynyl, wherein the C_1-C_6 alkyl, C_2-C_6 alkenyl, and C_2-C_6 alkynyl are each optionally substituted with 1, 2, or 3 independently selected halo substituents;

R^6 is C_1-C_6 alkyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, or 5-10 membered heteroaryl, wherein the C_1-C_6 alkyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, and 5-10 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1-C_6 alkyl, and OH; and

R^7 is C_1-C_6 alkyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, or 5-10 membered heteroaryl, wherein the C_1-C_6 alkyl, C_3-C_8 cycloalkyl, 4-10 membered heterocycloalkyl, C_6-C_{10} aryl, and 5-10 membered heteroaryl are each optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1-C_6 alkyl, and OH; or

R^6 and R^7, together with the nitrogen atom to which they are attached, form a 4-7 membered heterocyclyl, wherein the 4-7 membered heterocyclyl is optionally substituted with 1, 2, or 3 substituents independently selected from the group consisting of halo, C_1-C_6 alkyl, and OH.

19. A pharmaceutical composition comprising a compound of any one of claims 1-18, or a pharmaceutically acceptable salt or tautomer thereof, and at least one pharmaceutically acceptable excipient.

20. An *in vitro* method for inhibiting tyrosine kinase activity in a cell, comprising contacting the cell with an effective amount of a compound of any one of claims 1-18, or a

pharmaceutically acceptable salt or tautomer thereof, wherein the tyrosine kinase is selected from the group consisting of Abelson homolog 1, Abelson homolog 2, and breakpoint cluster region-Abelson homolog 1.

21. Use of a compound of any one of claims 1-18, or a pharmaceutically acceptable salt or tautomer thereof, for the manufacture of a medicament for inhibiting tyrosine kinase activity in a patient in need thereof, wherein the tyrosine kinase is selected from the group consisting of Abelson protein, Abelson-related protein, and breakpoint cluster region-Abelson protein.

22. The use according to claim 21, wherein the patient has a disease selected from the group consisting of leukemia, Alzheimer's disease, and Parkinson's disease.

23. Use of a compound of any one of claims 1-18, or a pharmaceutically acceptable salt or tautomer thereof, for the manufacture of a medicament for treating leukemia in a patient in need thereof, wherein the leukemia is selected from the group consisting of acute lymphoblastic leukemia, acute myeloid leukemia, and chronic myeloid leukemia.

24. The use according to claim 23, wherein:

(a) the leukemia is selected from the group consisting of acute lymphoblastic leukemia and chronic myeloid leukemia; and

(b) the medicament further comprises a therapeutically effective amount of a compound selected from the group consisting of bafetinib, bosutinib, dasatinib, imatinib, nilotinib, and ponatinib.

25. The use according to claim 23, wherein the chronic myeloid leukemia is resistant to standard-of-care treatment.

26. The use according to claim 23, wherein the chronic myeloid leukemia is resistant to treatment with a compound selected from the group consisting of dasatinib, imatinib, and nilotinib, or a combination thereof.

27. The use according to claim 23, wherein the acute myeloid leukemia is secondary acute myeloid leukemia.

28. A compound of any one of claims 1-18, or a pharmaceutically acceptable salt or tautomer thereof, for use in inhibiting tyrosine kinase activity in a patient in need thereof, wherein the tyrosine kinase is selected from the group consisting of Abelson protein, Abelson-related protein, and breakpoint cluster region-Abelson protein.

29. The compound according to claim 28, wherein the patient has a disease selected from the group consisting of leukemia, Alzheimer's disease, and Parkinson's disease.

30. A compound of any one of claims 1-18, or a pharmaceutically acceptable salt or tautomer thereof, for use in treating leukemia in a patient in need thereof, wherein the leukemia is selected from the group consisting of acute lymphoblastic leukemia, acute myeloid leukemia, and chronic myeloid leukemia.

31. The compound according to claim 30, wherein:

(a) the leukemia is selected from the group consisting of acute lymphoblastic leukemia and chronic myeloid leukemia; and

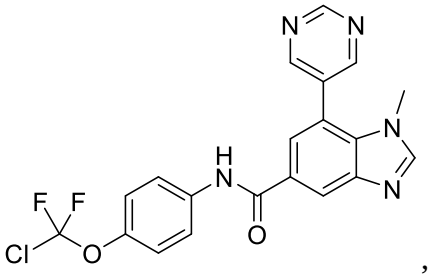
(b) the treatment further comprises a therapeutically effective amount of a compound selected from the group consisting of bafetinib, bosutinib, dasatinib, imatinib, nilotinib, and ponatinib.

32. The compound according to claim 30, wherein the chronic myeloid leukemia is resistant to standard-of-care treatment.

33. The compound according to claim 30, wherein the chronic myeloid leukemia is resistant to treatment with a compound selected from the group consisting of dasatinib, imatinib, and nilotinib, or a combination thereof.

34. The compound according to claim 30, wherein the acute myeloid leukemia is secondary acute myeloid leukemia.

35. A compound selected from the group consisting of: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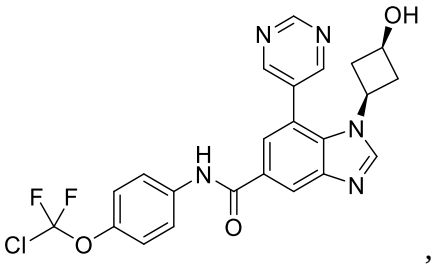
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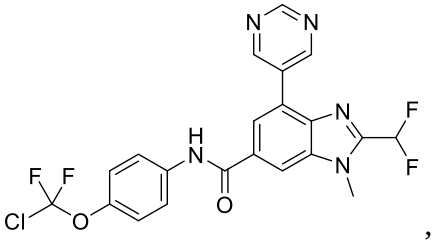
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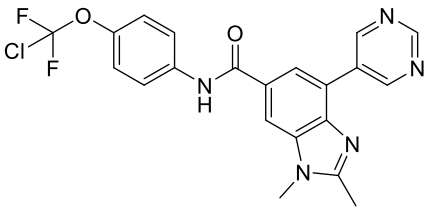
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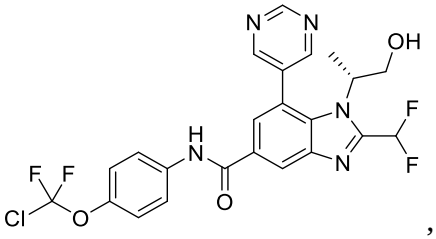
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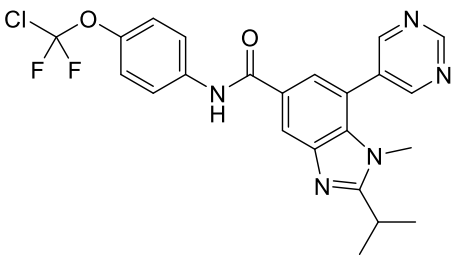
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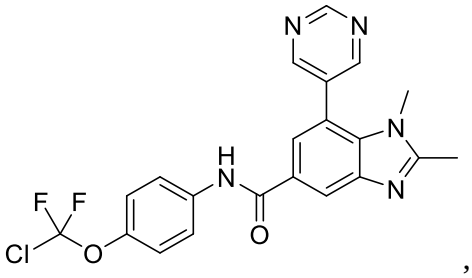
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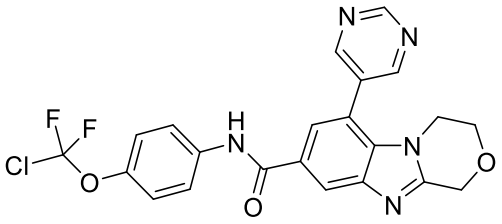
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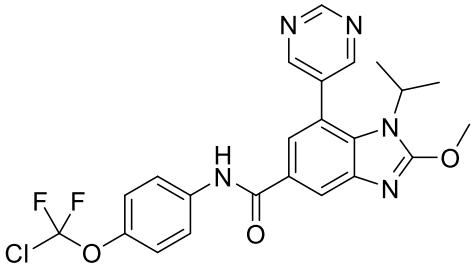
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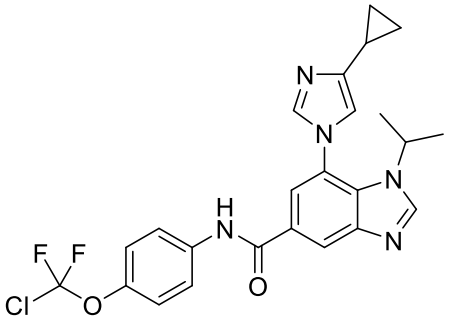
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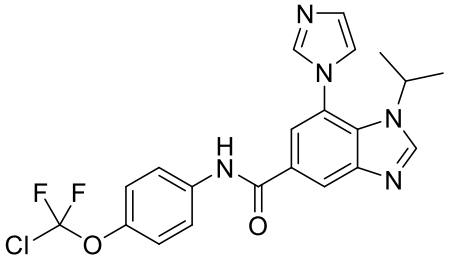
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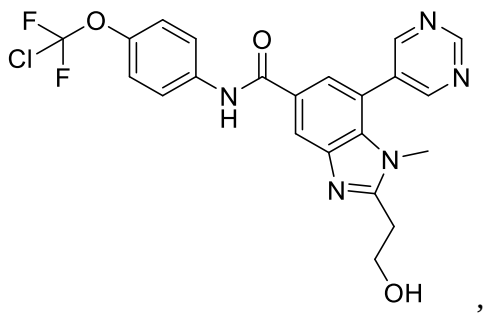
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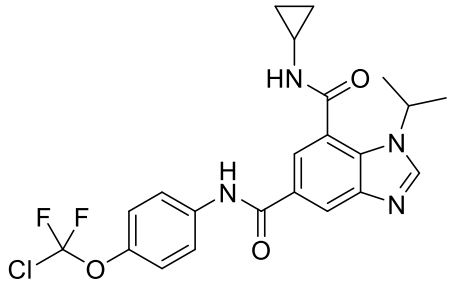
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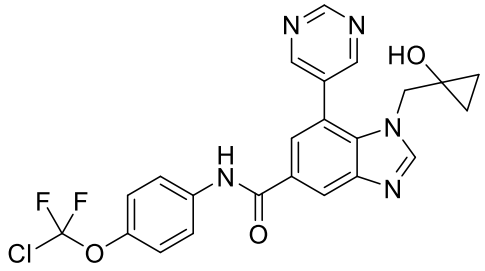
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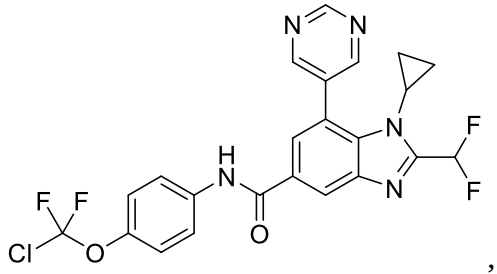
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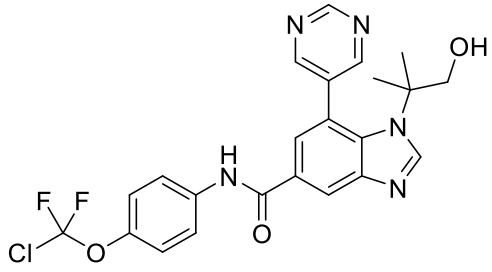
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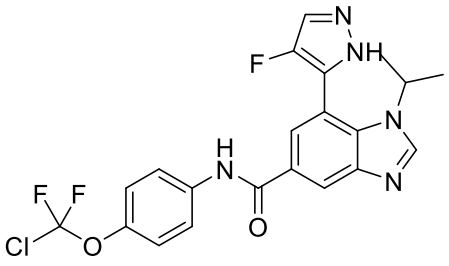
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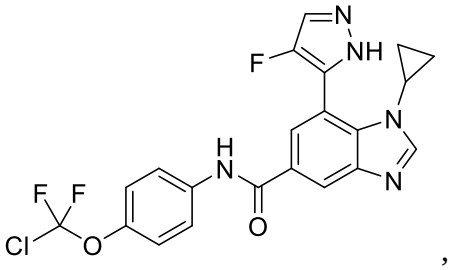
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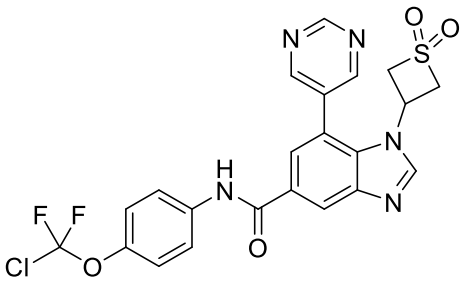
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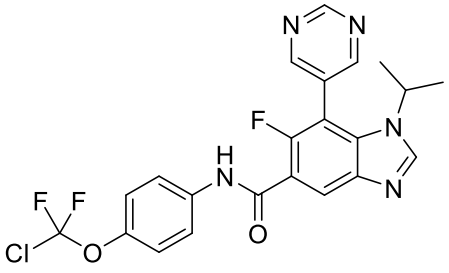
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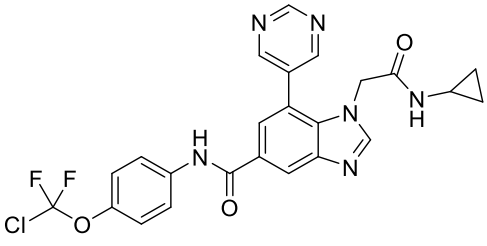
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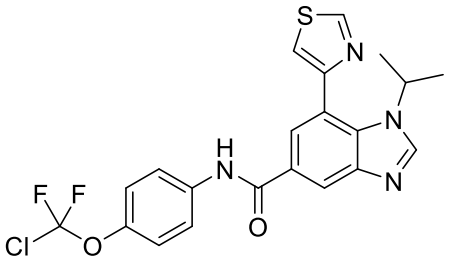
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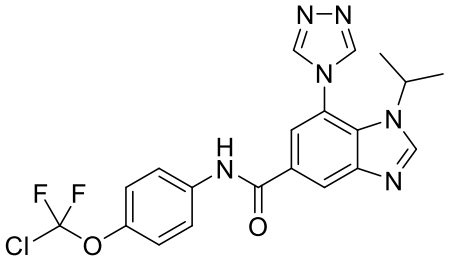
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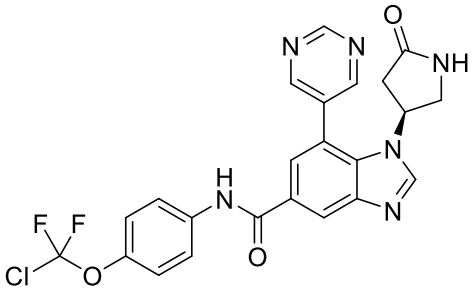
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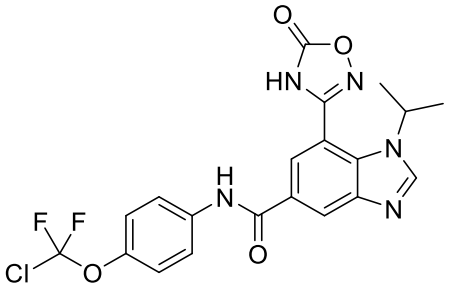
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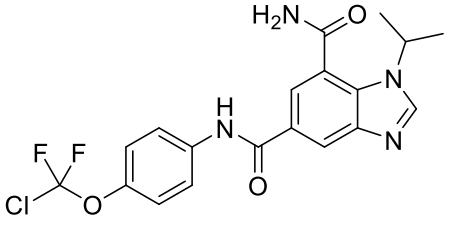
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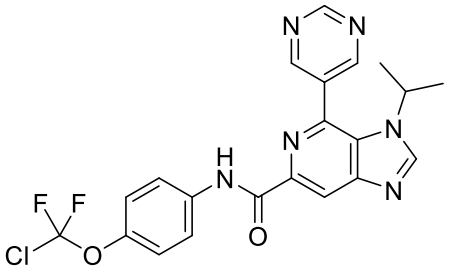
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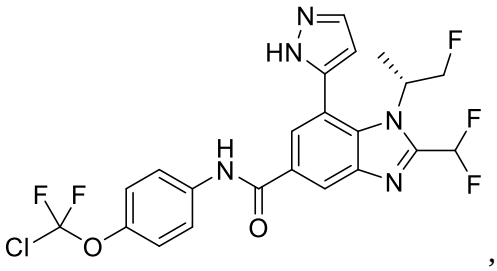
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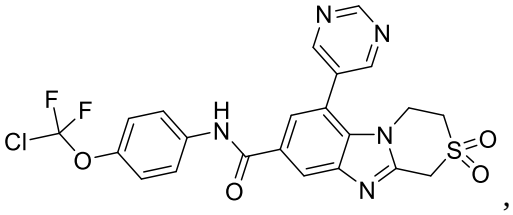
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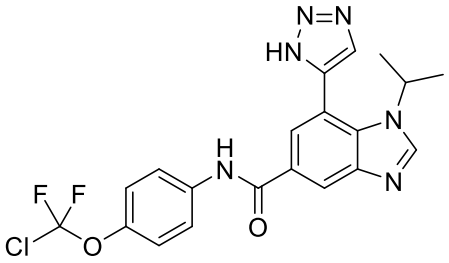
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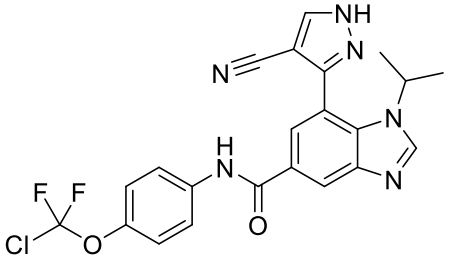
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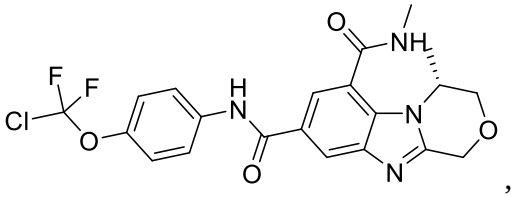
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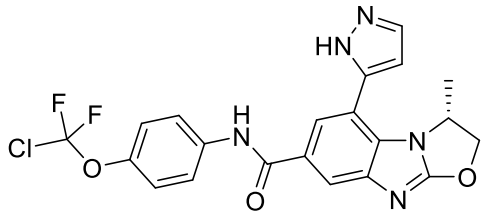
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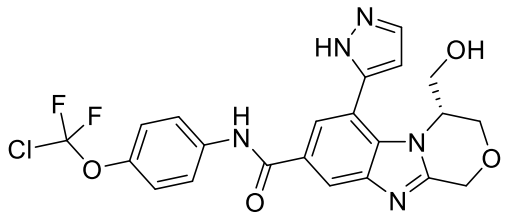
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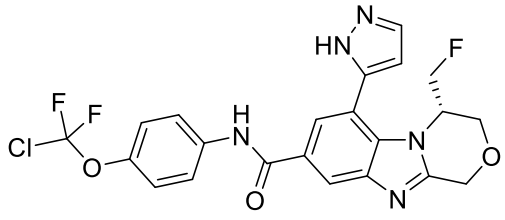
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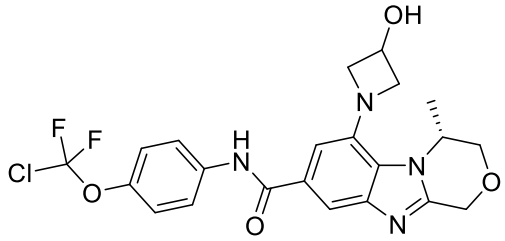
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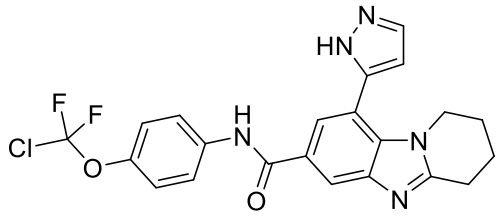
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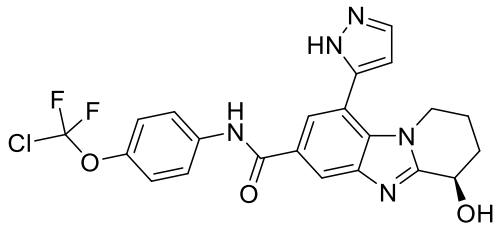
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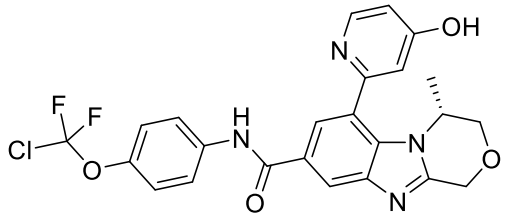
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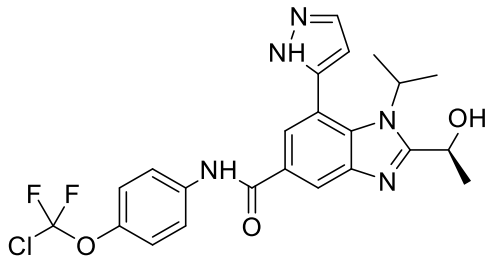
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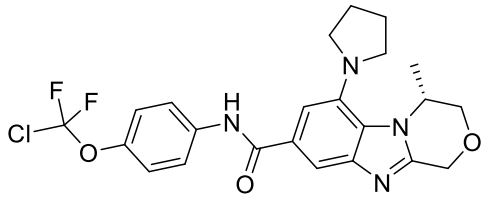
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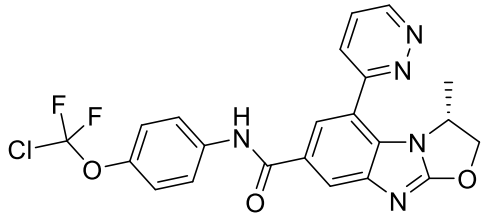
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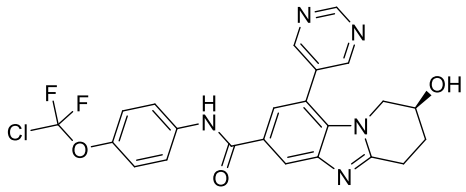
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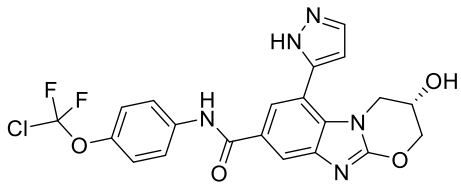
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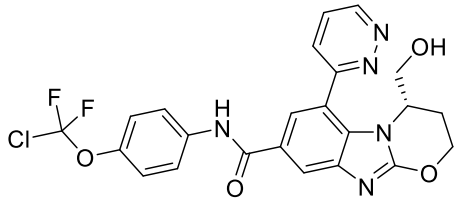
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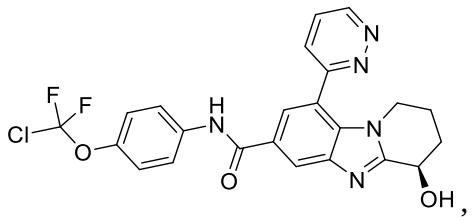
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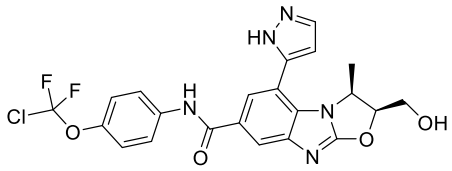
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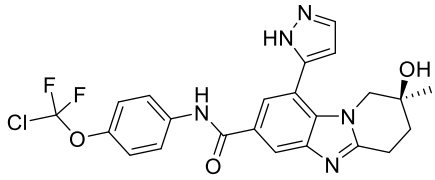
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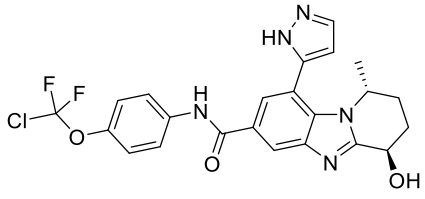
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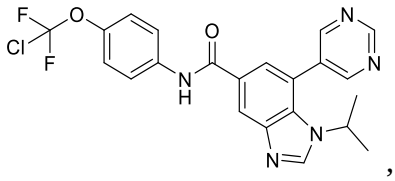
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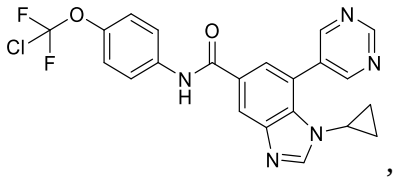
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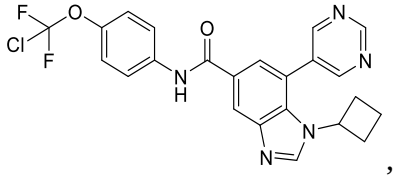
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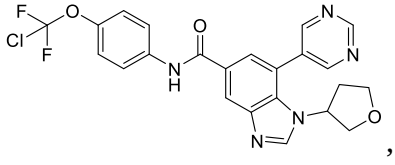
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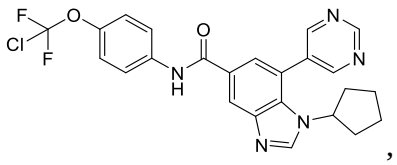
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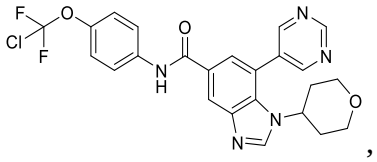
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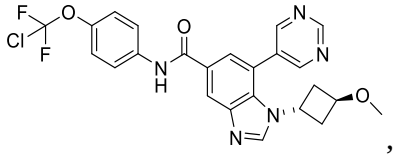
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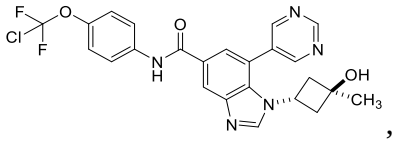
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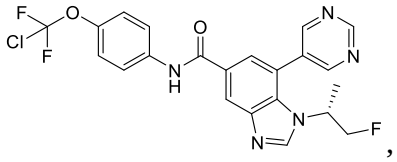
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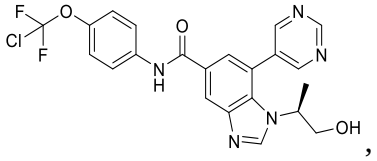
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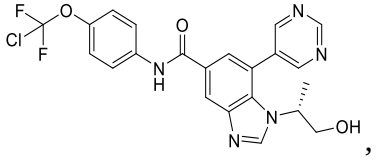
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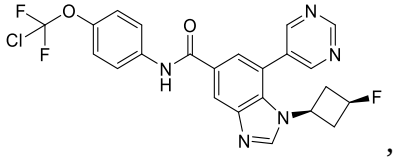
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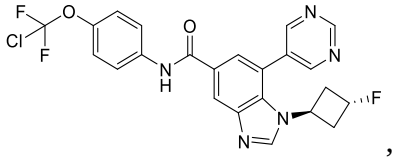
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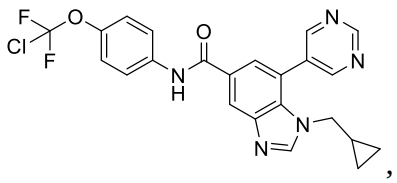

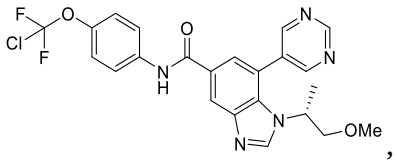

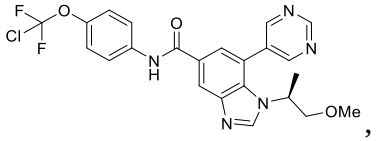

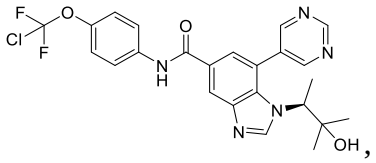

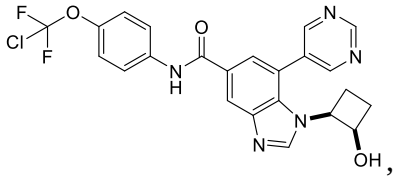

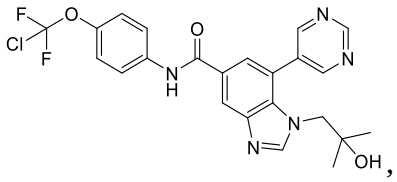

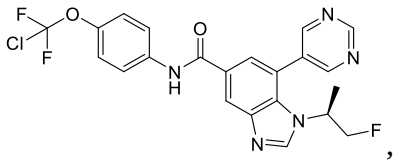

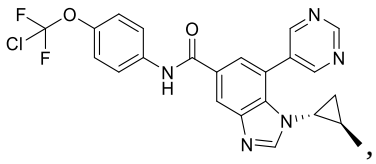

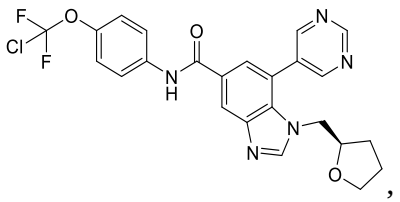
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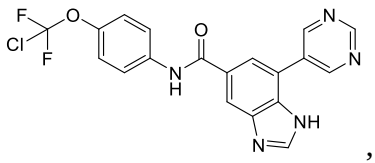
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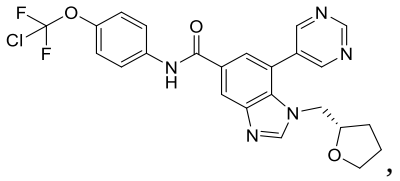
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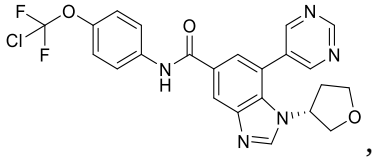
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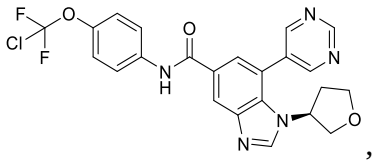
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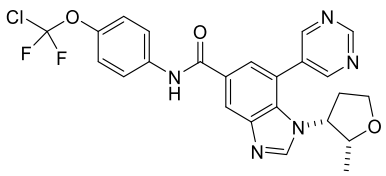
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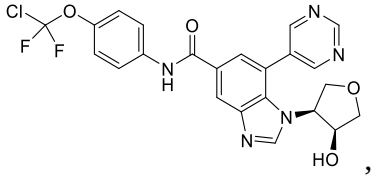
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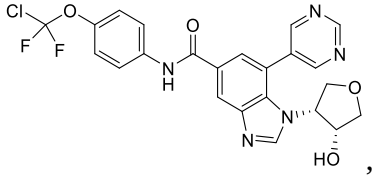
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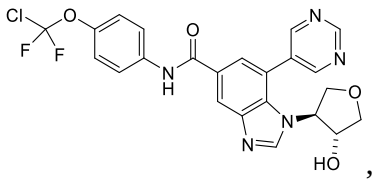
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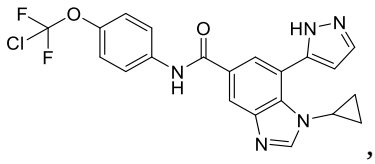
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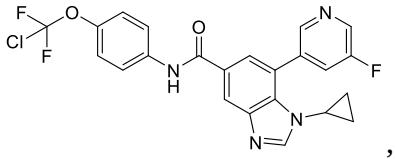
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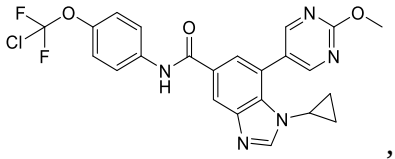
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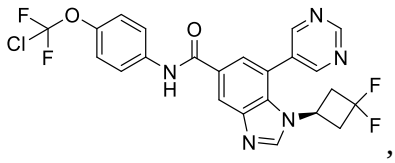
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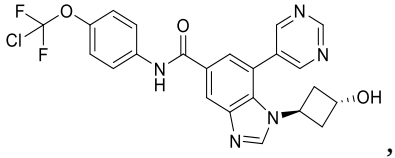
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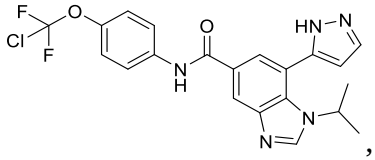
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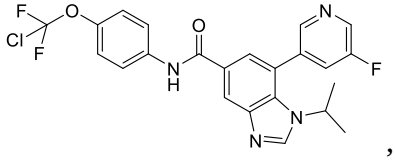
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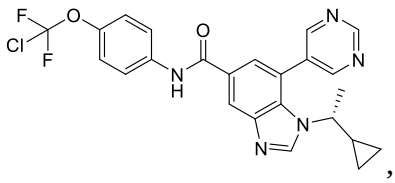
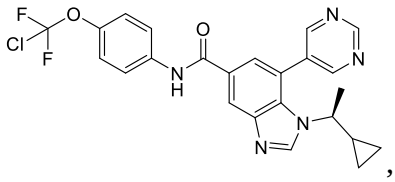
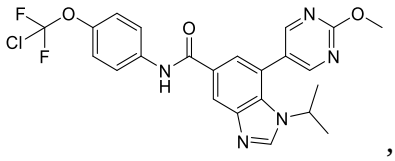
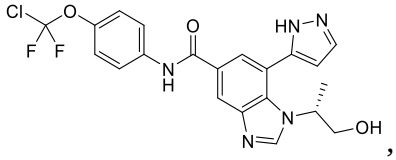
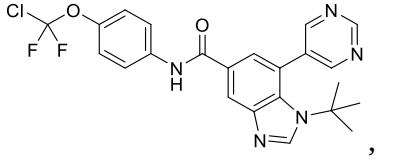
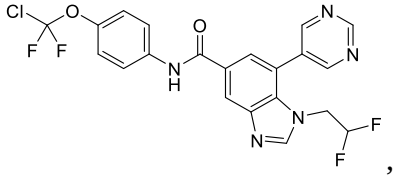
,

,

,

,

,

,

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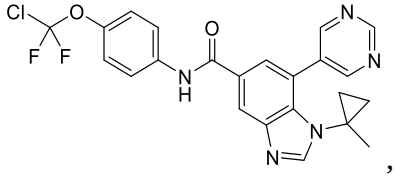
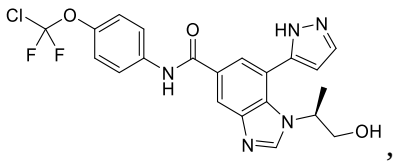
,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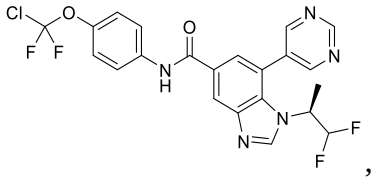
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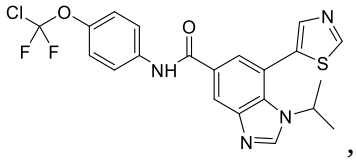
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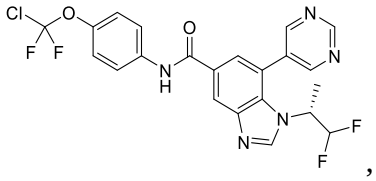
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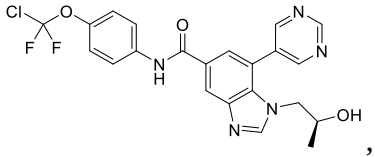
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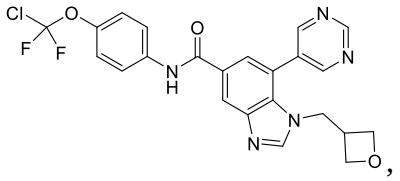
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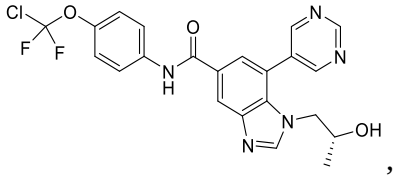
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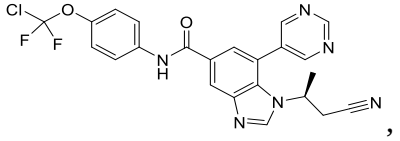
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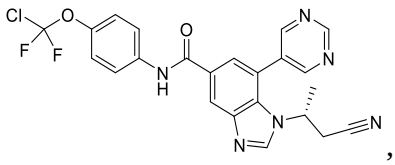
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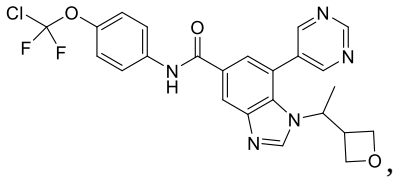
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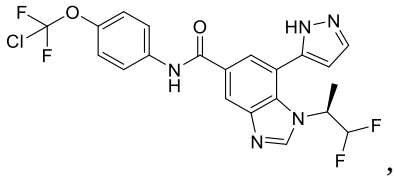
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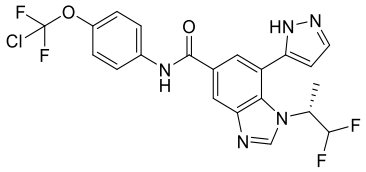
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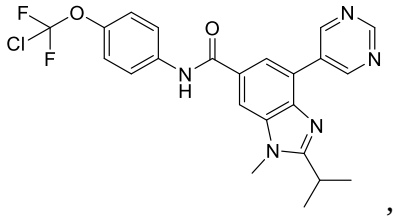
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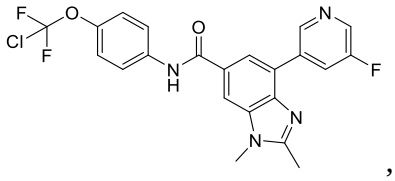
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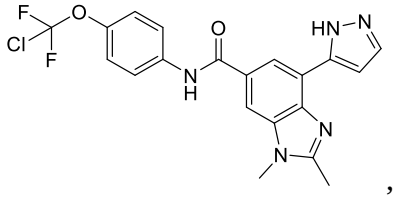
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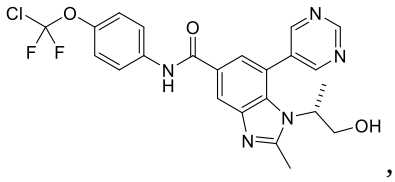
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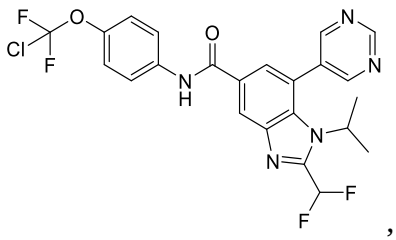
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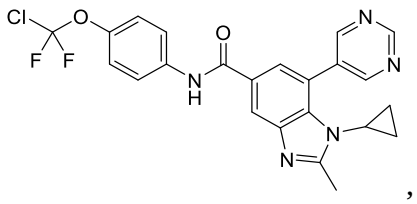
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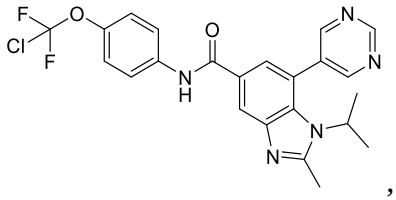
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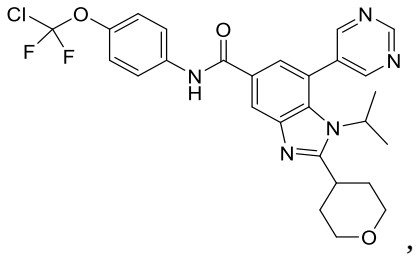
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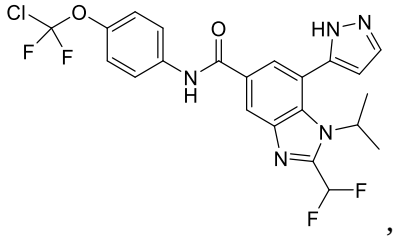
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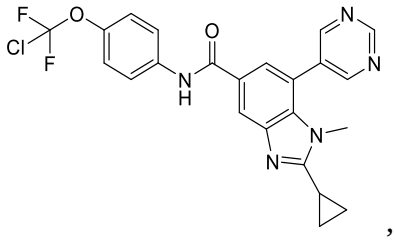
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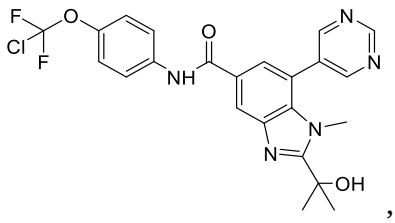
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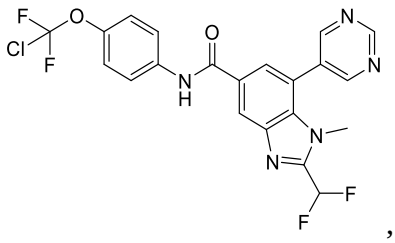
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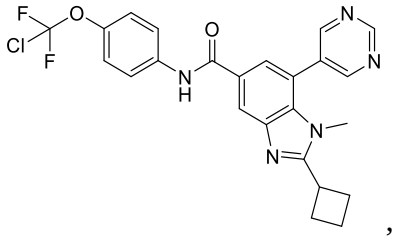
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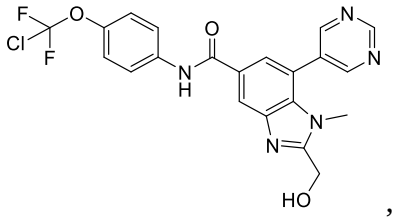
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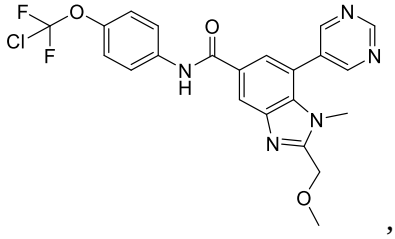
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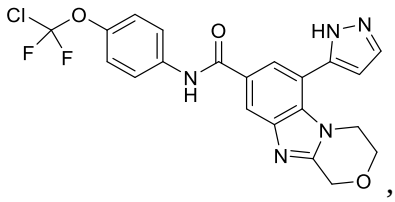
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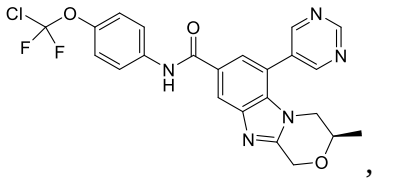
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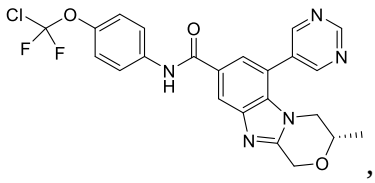
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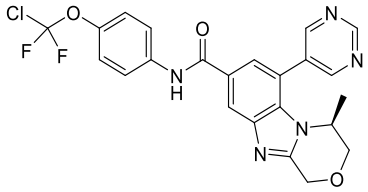
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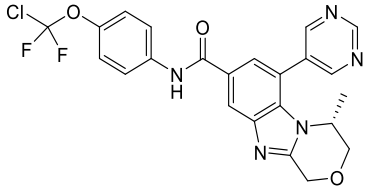
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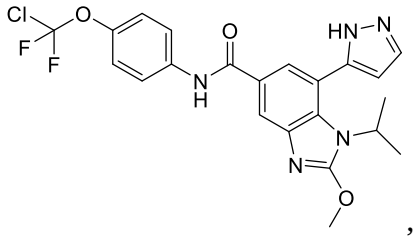
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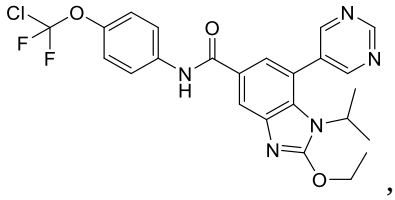
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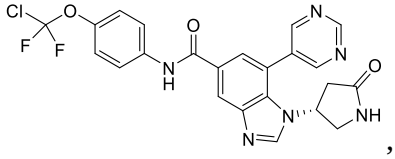
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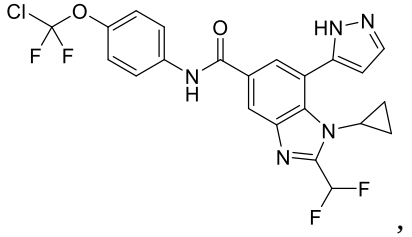
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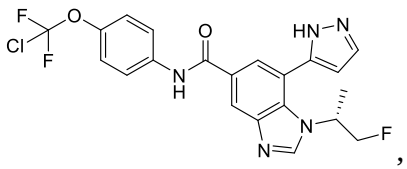
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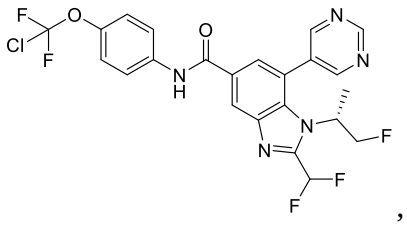
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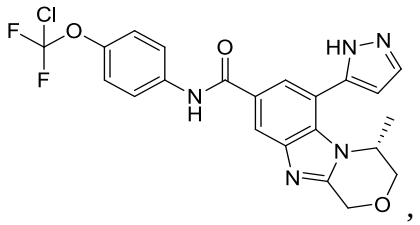
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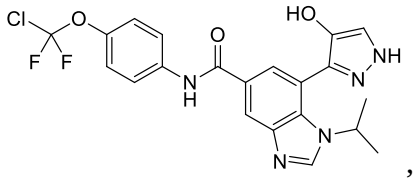
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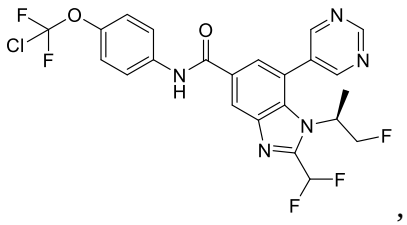
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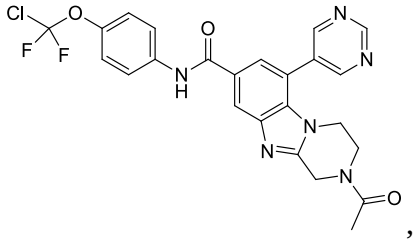
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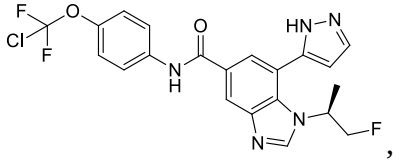
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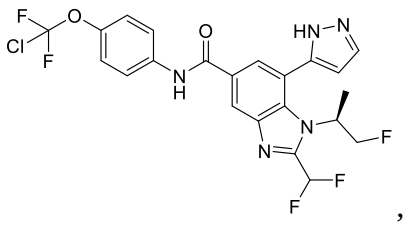
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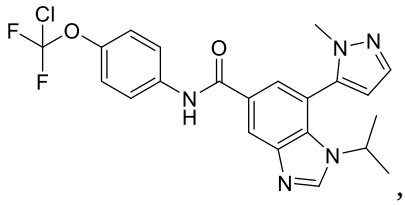
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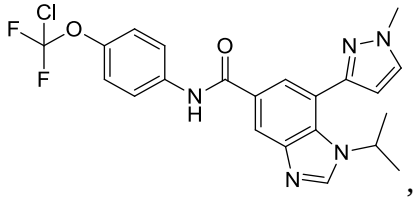
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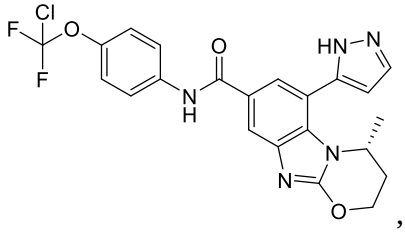
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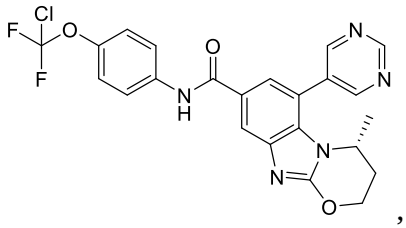
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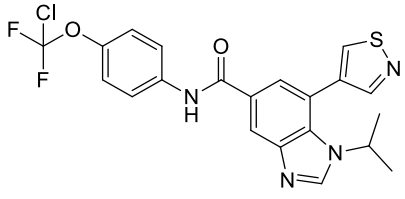
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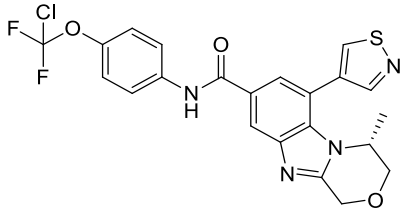
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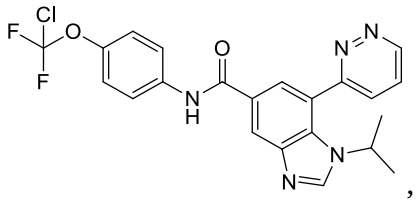
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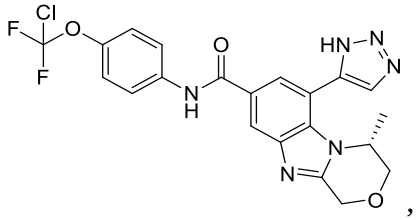
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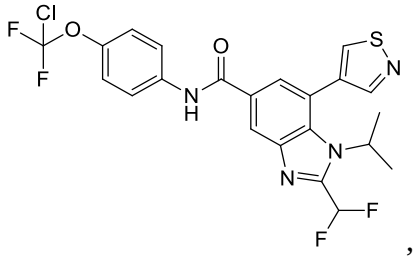
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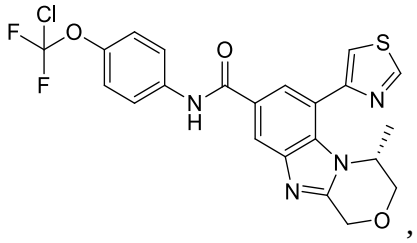
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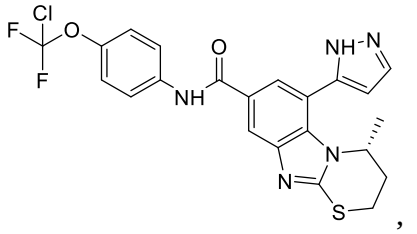
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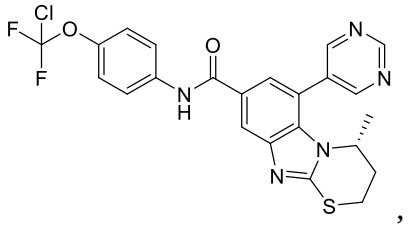
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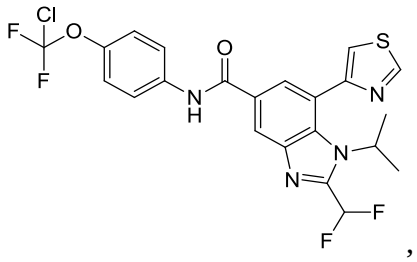
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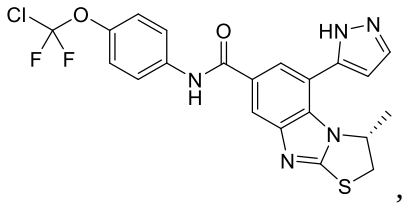
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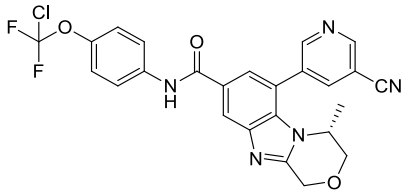
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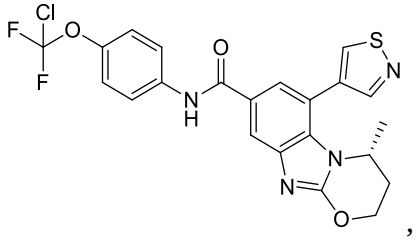
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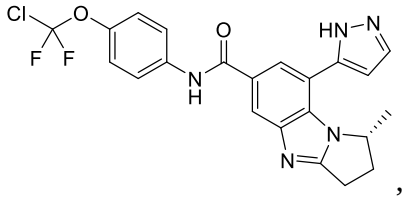
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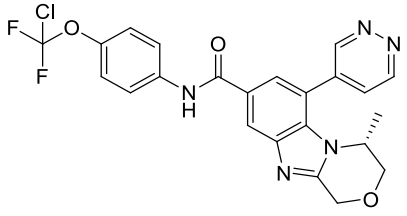
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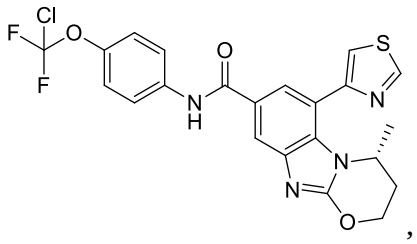
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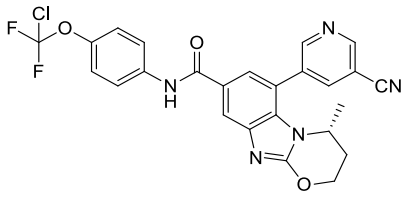
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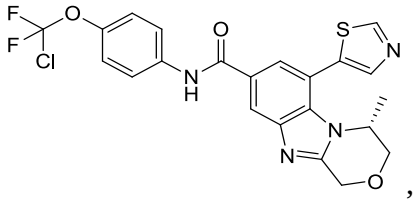
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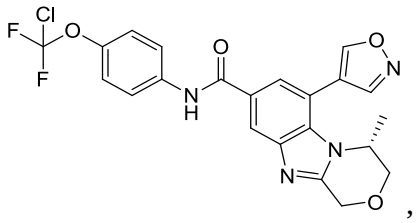
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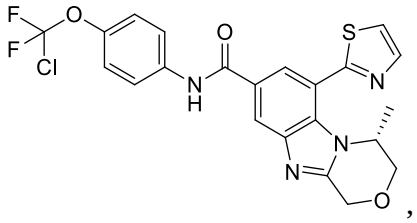
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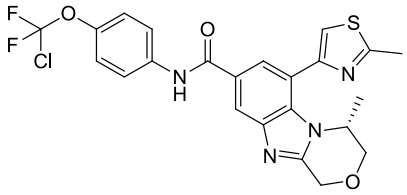
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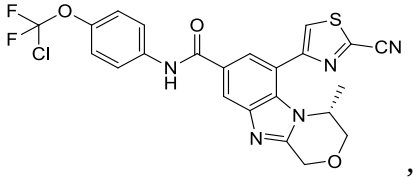
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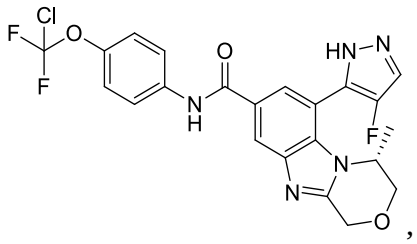
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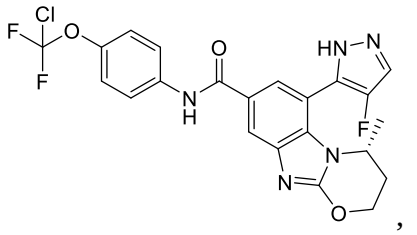
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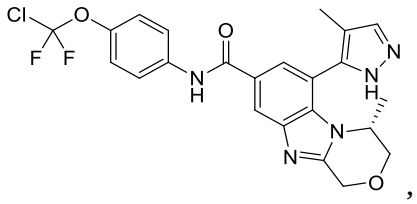
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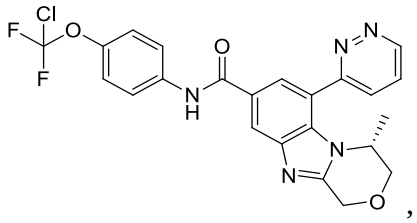
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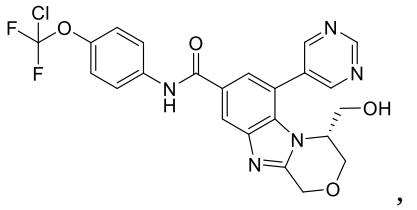
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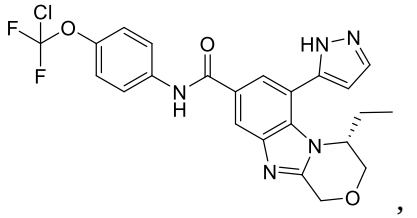
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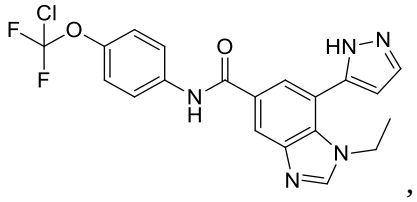
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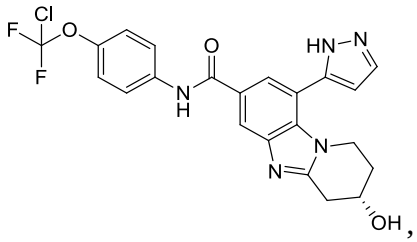
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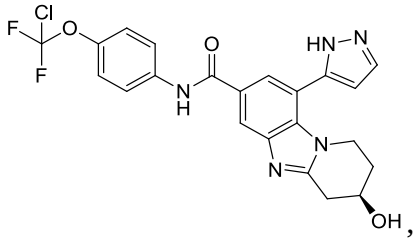
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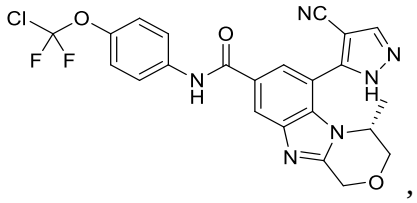
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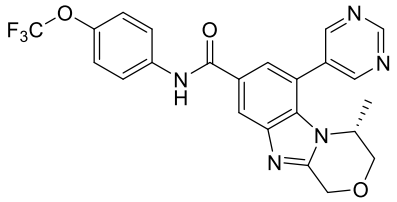
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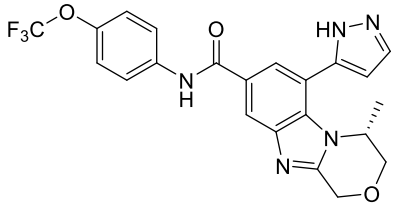
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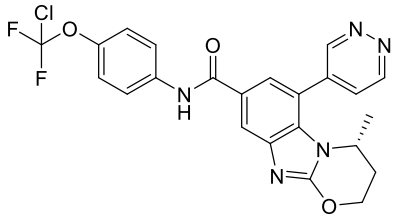
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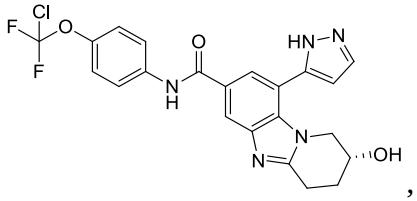
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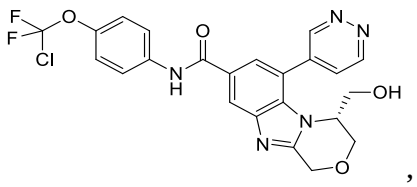
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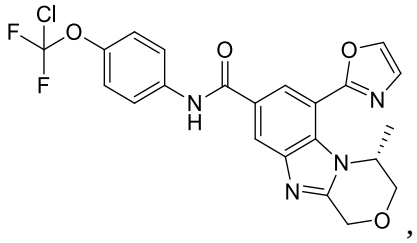
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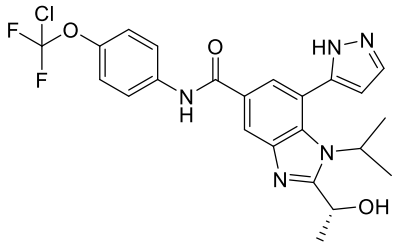
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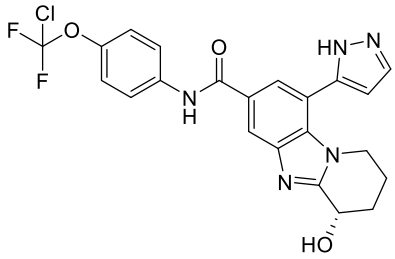
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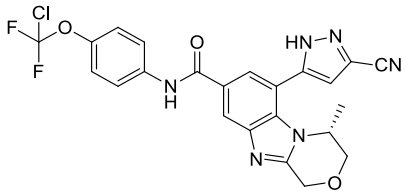
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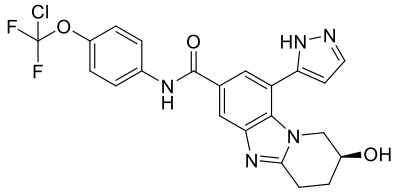
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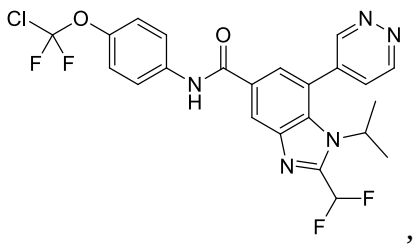
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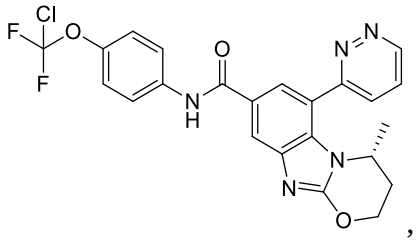
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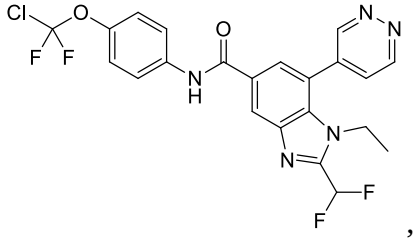
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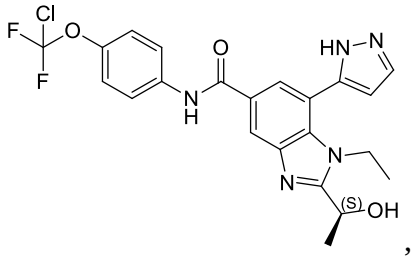
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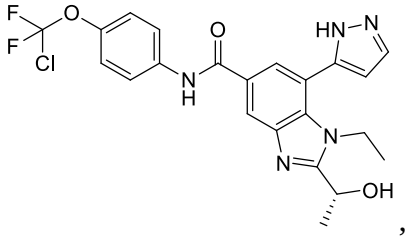
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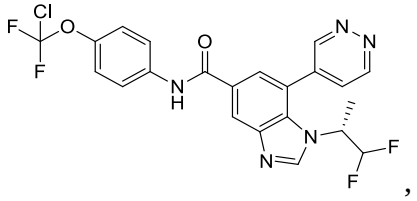
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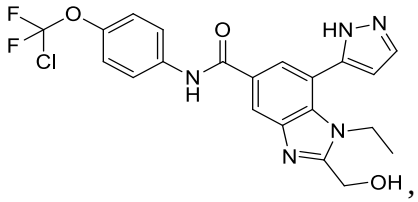
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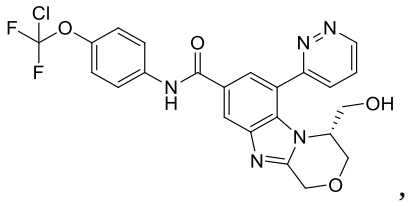
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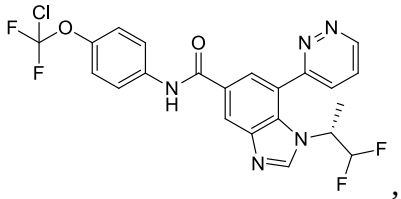
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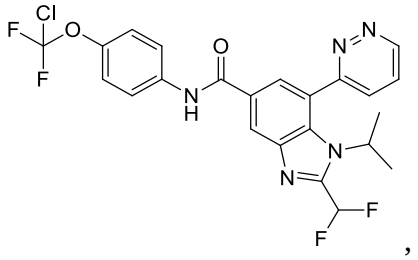
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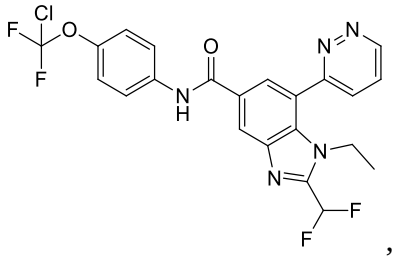
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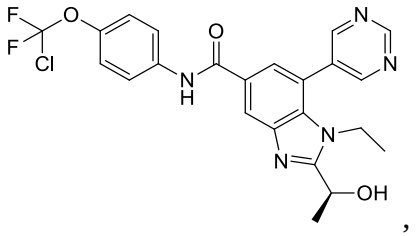
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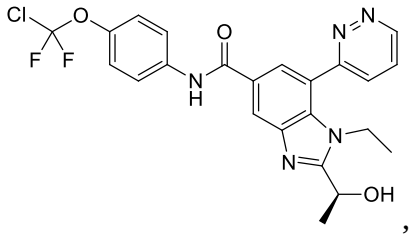
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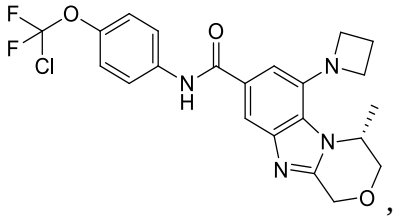
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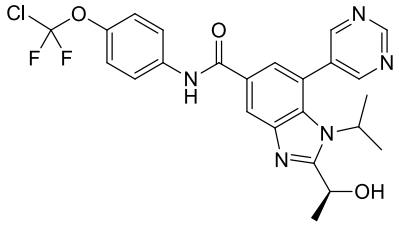
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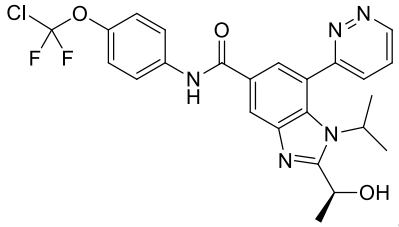
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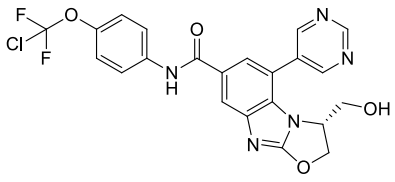
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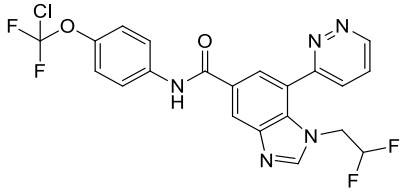
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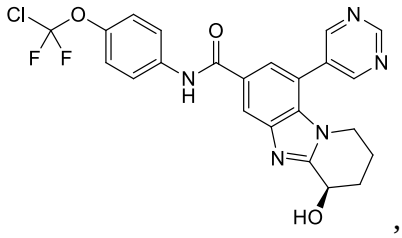
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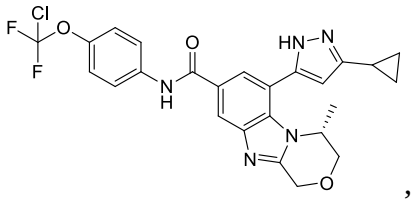
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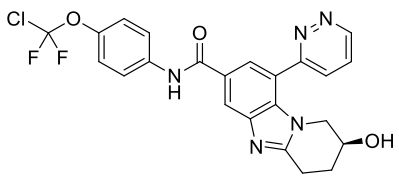
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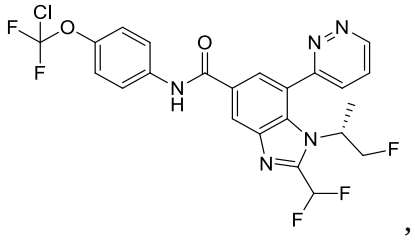
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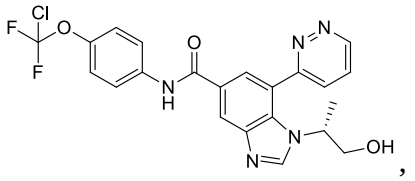
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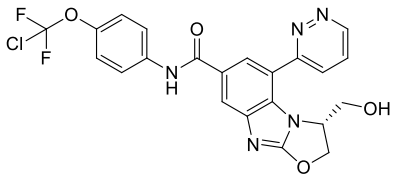
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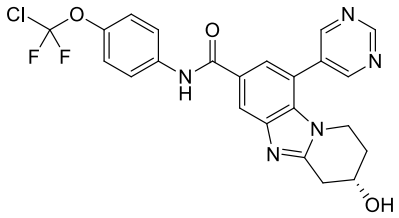
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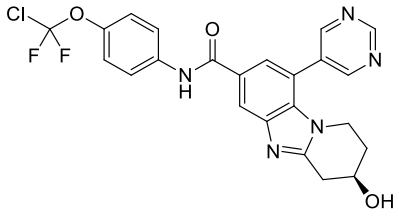
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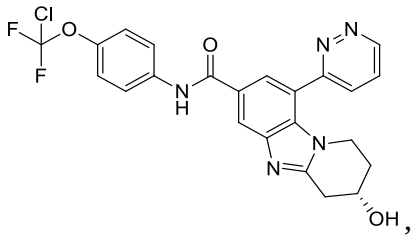
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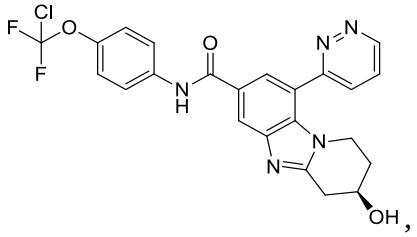
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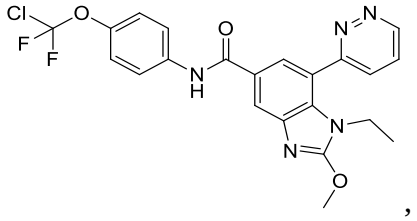
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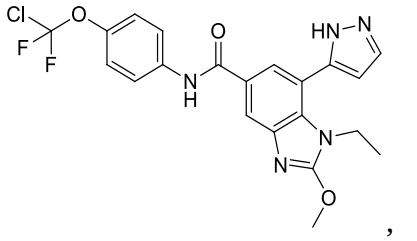
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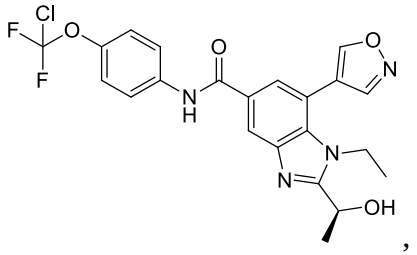
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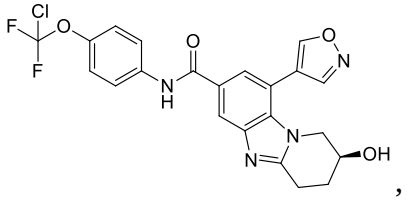
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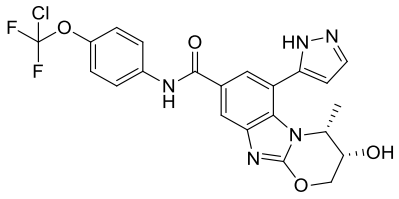
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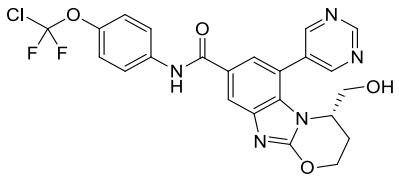
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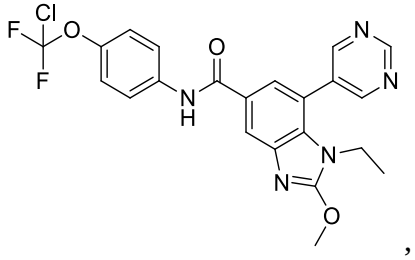
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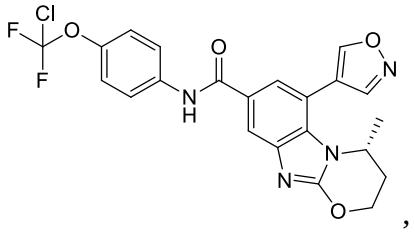
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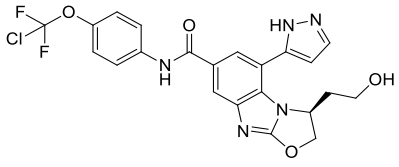
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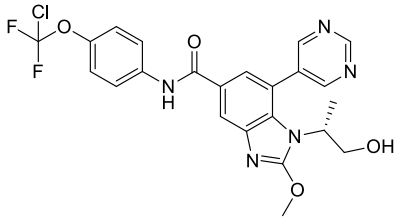
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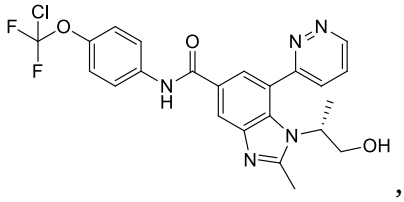
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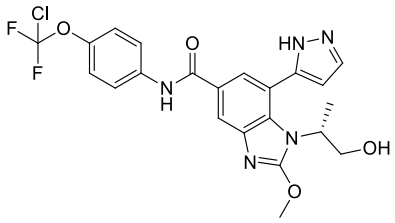
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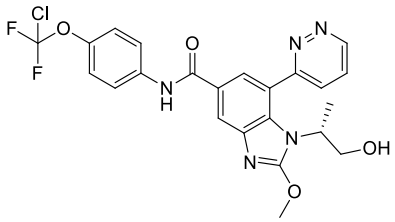
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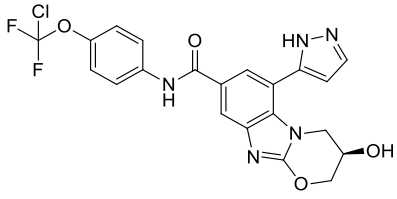
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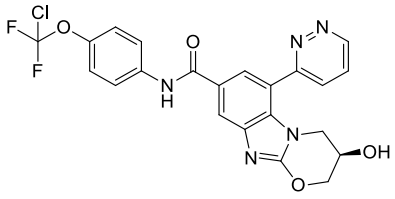
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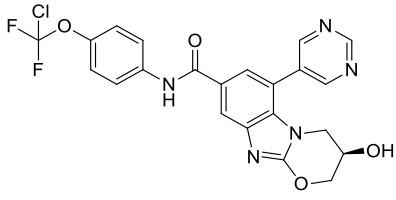
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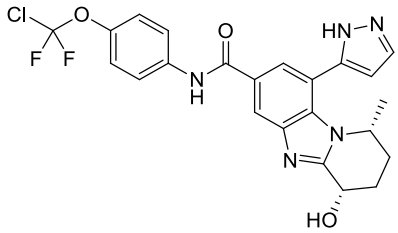
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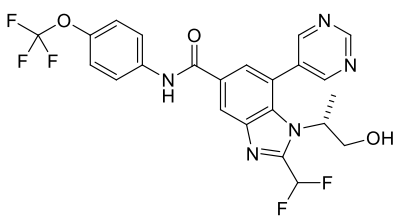
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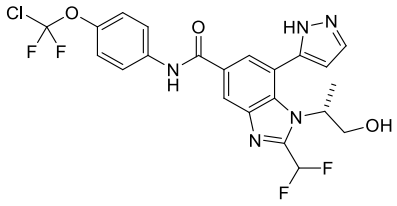
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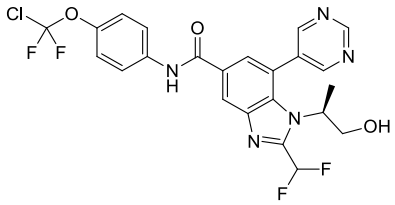
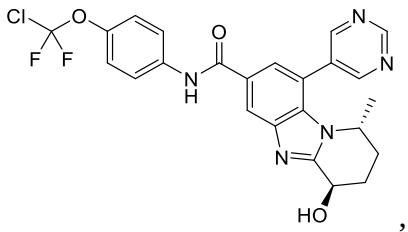
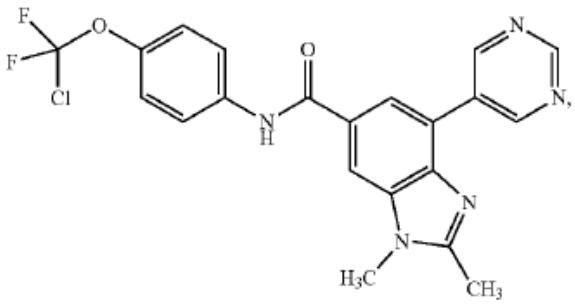
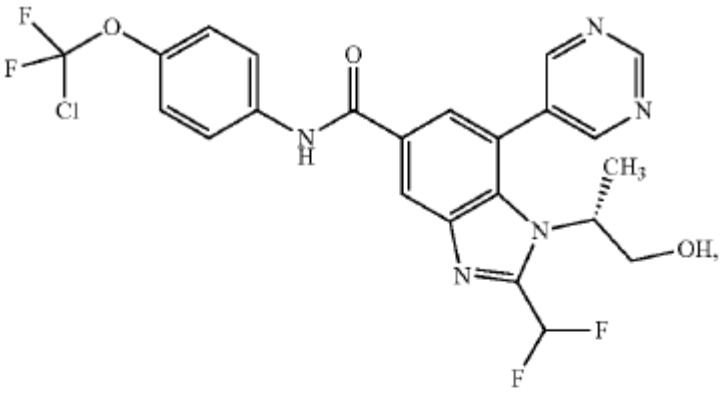

, and

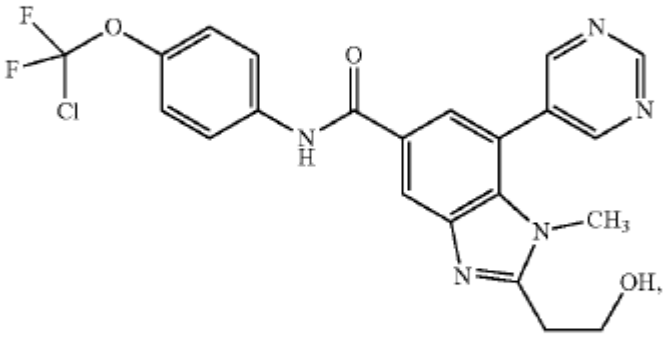

,

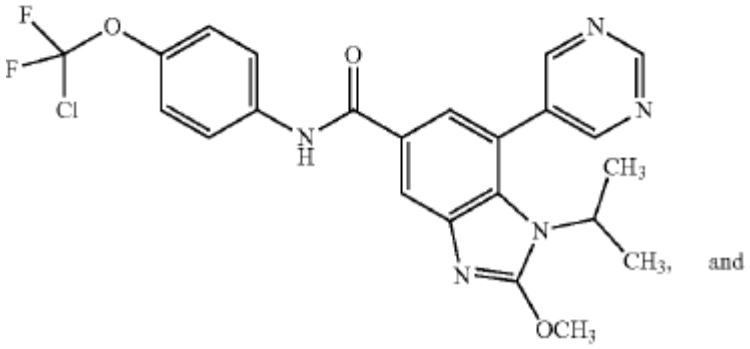
or a pharmaceutically acceptable salt or tautomer thereof.

36. The compound of claim 35, wherein the compound is selected from the group consisting of:

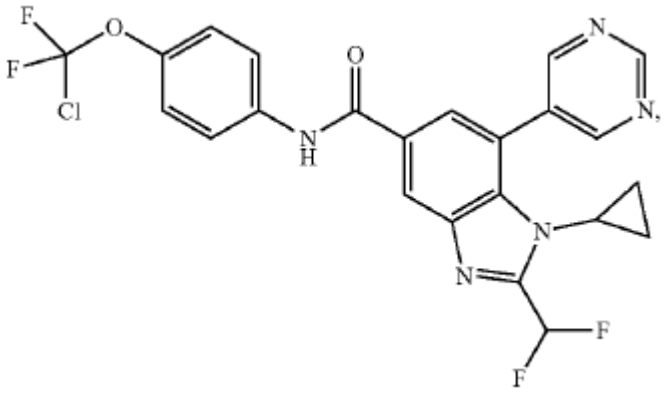






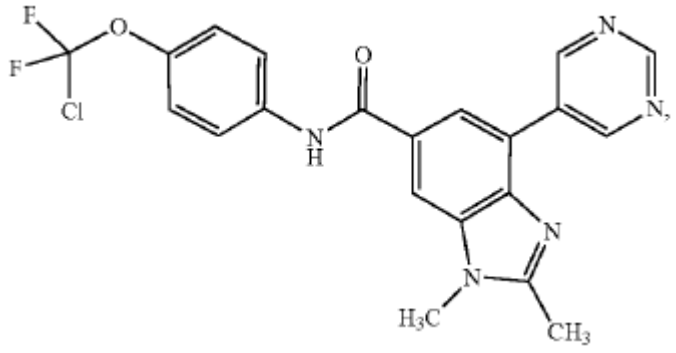


and



or a pharmaceutically acceptable salt or tautomer thereof.

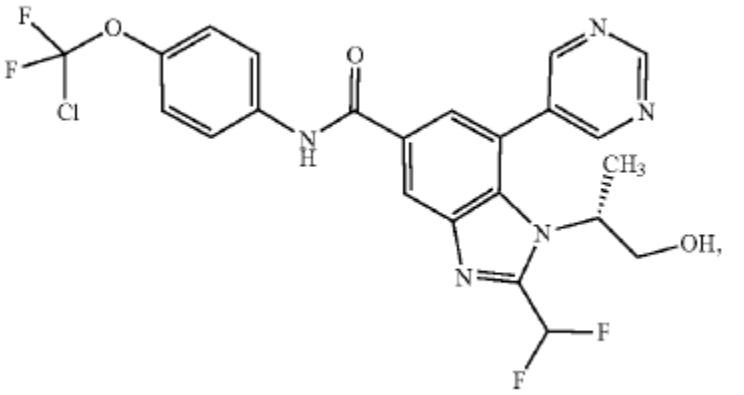
37. The compound of claim 36, wherein the compound is:



,

or a pharmaceutically acceptable salt or tautomer thereof.

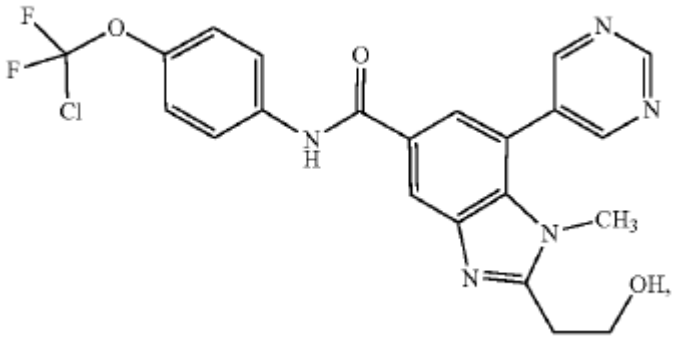
38. The compound of claim 36, wherein the compound is:



,

or a pharmaceutically acceptable salt or tautomer thereof.

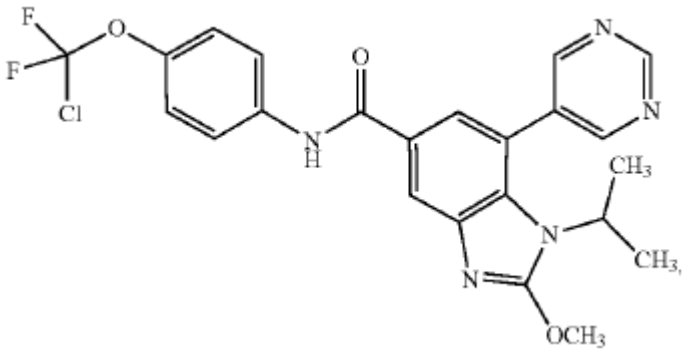
39. The compound of claim 36, wherein the compound is:



,

or a pharmaceutically acceptable salt or tautomer thereof.

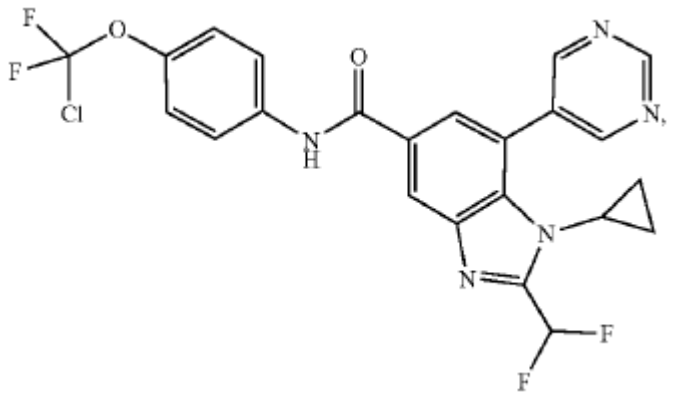
40. The compound of claim 36, wherein the compound is:



,

or a pharmaceutically acceptable salt or tautomer thereof.

41. The compound of claim 36, wherein the compound is:



,

or a pharmaceutically acceptable salt or tautomer thereof.

42. A pharmaceutical composition comprising a compound of any one of claims 35-41, or a pharmaceutically acceptable salt or tautomer thereof, and at least one pharmaceutically acceptable excipient.

43. An *in vitro* method for inhibiting tyrosine kinase activity in a cell, comprising contacting the cell with an effective amount of a compound of any one of claims 35-41, or a pharmaceutically acceptable salt or tautomer thereof, wherein the tyrosine kinase is selected from the group consisting of Abelson homolog 1, Abelson homolog 2, and breakpoint cluster region-Abelson homolog 1.

44. Use of a compound of any one of claims 35-41, or a pharmaceutically acceptable salt or tautomer thereof, for the manufacture of a medicament for inhibiting tyrosine kinase activity in a patient in need thereof, wherein the tyrosine kinase is selected from the group consisting of Abelson protein, Abelson-related protein, and breakpoint cluster region-Abelson protein.

45. The use according to claim 44, wherein the patient has a disease selected from the group consisting of leukemia, Alzheimer's disease, and Parkinson's disease.

46. Use of a compound of any one of claims 35-41, or a pharmaceutically acceptable salt or tautomer thereof, for the manufacture of a medicament for treating leukemia in a patient in need thereof, wherein the leukemia is selected from the group consisting of acute lymphoblastic leukemia, acute myeloid leukemia, and chronic myeloid leukemia.

47. The use according to claim 46, wherein:

(a) the leukemia is selected from the group consisting of acute lymphoblastic leukemia and chronic myeloid leukemia; and

(b) the medicament further comprises a therapeutically effective amount of a compound selected from the group consisting of bafetinib, bosutinib, dasatinib, imatinib, nilotinib, and ponatinib.

48. The use according to claim 46, wherein the chronic myeloid leukemia is resistant to standard-of-care treatment.

49. The use according to claim 46, wherein the chronic myeloid leukemia is resistant to treatment with a compound selected from the group consisting of dasatinib, imatinib, and nilotinib, or a combination thereof.

50. The use according to claim 46, wherein the acute myeloid leukemia is secondary acute myeloid leukemia.

51. A compound of any one of claims 35-41, or a pharmaceutically acceptable salt or tautomer thereof, for use in inhibiting tyrosine kinase activity in a patient in need thereof, wherein the tyrosine kinase is selected from the group consisting of Abelson protein, Abelson-related protein, and breakpoint cluster region-Abelson protein.

52. The compound according to claim 51, wherein the patient has a disease selected from the group consisting of leukemia, Alzheimer's disease, and Parkinson's disease.

53. A compound of any one of claims 35-41, or a pharmaceutically acceptable salt or tautomer thereof, for use in treating leukemia in a patient in need thereof, wherein the leukemia is selected from the group consisting of acute lymphoblastic leukemia, acute myeloid leukemia, and chronic myeloid leukemia.

54. The compound according to claim 53, wherein:

(a) the leukemia is selected from the group consisting of acute lymphoblastic leukemia and chronic myeloid leukemia; and

(b) the treatment further comprises a therapeutically effective amount of a compound selected from the group consisting of bafetinib, bosutinib, dasatinib, imatinib, nilotinib, and ponatinib.

55. The compound according to claim 54, wherein the chronic myeloid leukemia is resistant to standard-of-care treatment.

56. The compound according to claim 54, wherein the chronic myeloid leukemia is resistant to treatment with a compound selected from the group consisting of dasatinib, imatinib, and nilotinib, or a combination thereof.

57. The compound according to claim 54, wherein the acute myeloid leukemia is secondary acute myeloid leukemia.